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LOW RESERVE KIDNEY*

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OUR knowledge of renal physiology has increased considerably during the past ten years, due greatly to the efforts of Richards, Marshall, Rehberg, and others. It seems well established today that filtration is the sole function of the kidney glomerulus and that reabsorption is the predominant function of the tubule, but that tubular secretion does occur and, furthermore, that under certain conditions such secretion may play a very important rôle in renal function.

KIDNEY FUNCTION

In order that glomerular filtration may occur, it is essential that the blood pressure in the capillaries of the glomerulus be greater than the osmotic pressure of the proteins in the blood plus the intracapsular pressure of the glomerulus. This pressure, necessary for glomerular function, has been called the "effective filtration pressure." It is, of course, clear that such filtration is further dependent upon the rate of blood flow through the kidney, in other words the rate at which new blood is brought in contact with the endothelium of the glomeruli. The other two factors that influence filtration are the area of the surface for filtration, that is, the number and size of capillary channels in the glomeruli, and the actual permeability of the glomerular membrane.

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PATHOLOGIC CONDITIONS

With this rather brief description of the present-day views of renal function, we may now turn to a consideration of a few of the factors involved in pathologic conditions affecting the kidneys.

It is quite evident that glomerular filtration will decrease if any one or more of the factors essential to filtration are affected. If the glomerular membrane be thickened, if the filtering surface be reduced in area by the partial or complete destruction of glomeruli, if the filtration pressure be reduced or if the rate of blood flow through the kidneys be decreased, glomerular filtration will be impaired. Similarly, increased or decreased permeability of the tubular wall will bring about changes in the rate and amount of water, chlorides and sugar reabsorbed, in the amount of back diffusion of urea and other substances, as well as in the ability of the tubules to secrete substances such as ammonia and hippuric acid.

It is equally evident that in the nephropathies, acute glomerulonephritis, chronic glomerulonephritis, arteriosclerotic chronic nephritis and nephrosis, some of these factors are to a lesser or greater extent involved and so kidney function affected. The filtration rate, as shown by the urea filtration rate, may be decreased in acute nephritis, is markedly decreased in the terminal stages of chronic nephritis, whether of glomerulonephritic or arteriosclerotic origin, and may likewise be low in nephrosis. Rehberg found that also in essential hypertension there may be slight reduction in the filtration rate, even before albuminuria developed.

CHRONIC NEPHRITIS

Chronic nephritis may follow an acute glomerulonephritis or it may result from a general arteriosclerosis. It is well to point out that a sclerosis involving the renal arteries but not extending to the small arteries and the afferent glomerular arterioles, is usually not accompanied by kidney disease, but as soon as these arterioles become affected by the sclerosis, a persistent hypertension is present, with later involvement of heart, brain, and kidneys, and death may be due to renal insufficiency or apoplexy or coronary disease. The arteriolosclerosis is followed by a thickening of the capsular basement membrane ultimately resulting in a complete blockage or closure of the glomerulus and a disuse atrophy of the corresponding tubule. Primary or essential hypertension, undoubtedly starts as a generalized spasm of the arterioles, and it has been suggested that this hypertension, brought about by spasm, may later produce degeneration of the arterioles and so eventuate into a malignant or progressive renal disease. This type of hypertension is the so-called "red hypertension," in contrast to the "pale hypertension" (nephritic), where, according to Volhard,² the peripheral and retinal arteries are narrowed, albuminuric retinitis often present, and the con-

dition perhaps dependent on a pressor substance in the blood. Vollhard further believes that the "red hypertension" is not dependent on such pressure substances, but rather on a passive mechanism, based perhaps on early senescence of the arteries, a diminution of their muscular layer, overstretching of the elastic layer followed by an increased tonus of the arterioles.

The chronic nephritis complicating a pregnancy may, of course, be any of the above-stated forms, a chronic glomerulonephritis, or an arteriosclerotic chronic nephritis dependent upon arteriolar involvement, or one following essential hypertension (genuine or permanent) which has developed from a benign nephrangiosclerosis into actual and progressive kidney disease (malignant hypertension). Although it may not be absolutely essential for us to be able to differentiate between these various types, as they are present in a pregnant woman, it is most important to know that a chronic nephritis, however mild, is present, as this diseased condition is adversely affected by the pregnancy and good treatment demands termination of the pregnancy. We shall not discuss the details of diagnosis and treatment of chronic nephritis complicating pregnancy, as this has been done in earlier publications.^{3, 4}

LOW RESERVE KIDNEY

Renal reserve may be of two types, native and acquired, the latter usually following kidney operation, such as unilateral nephrectomy. Reference has already been made to the work of Richards and his co-workers on the variability of the extent of glomerular filtration surfaces and on the irregular velocity of blood flow through normal glomeruli. There appears to be great variability in the number of visibly functioning glomeruli, as observed under the microscope by these and other investigators. In 1924 Schmidt and Richards⁵ noted markedly different appearances in different glomeruli of the same kidney, one glomerular tuft perhaps showing many capillary channels through all of which blood is passing swiftly, while another may reveal only one capillary loop with blood passing through it. Furthermore, this picture may be constantly changing, due perhaps to vasoconstrictor or vasodilator stimuli. With such a variability of functioning glomeruli at any given time, and therefore a variability of the number of nonfunctioning or only partially functioning glomeruli, in the normal, it must be apparent that there is a large native reserve in the kidney, seldom called into play while the demands for excretion are at a normal base level. May not normal individuals differ in the extent of such native renal reserve, and may not even the same individual differ at different times in the amount of such reserve? It is a common observation that normal individuals with apparently normal kidneys may react very differently to every day stimuli, such as diuretics in the form of caffeine or water consumption. Diuresis

from drinking water is undoubtedly due to decreased tubular reabsorption. May not normal individuals also vary in their reaction to anti-diuretics, e.g., pituitrin?

In 1926, Stander and Peckham⁶ introduced the term "low reserve kidney" and defined it as follows:

1. An elevated blood pressure which at the end of the puerperium has dropped to a normal level. In most instances this elevation is not very marked, being approximately 150 systolic and 90 diastolic.

2. The amount of albumin in the urine is never very great, varying before delivery between a fraction of a gram and 2 gm. per liter, although the lower figures are most usually observed. The albumin disappears during the puerperium, and the patient leaves the service either with no albumin at all, or with at the most 0.1 gm. per liter.

3. The outstanding characteristic is the fact that in subsequent pregnancies, the patient's condition does not become aggravated, and she is as well as, or better than, in the preceding pregnancy.

4. The blood chemistry, as well as the urine chemistry, reveals nothing abnormal.

That the number of pregnancies through which the individual may go plays any rôle in the development of this entity is very doubtful, for the reason that we observe it particularly in primiparas although occasionally in all degrees of multiparas. Moreover, this type of kidney does not seem to be permanently injured by pregnancy. As the woman approaches term a certain amount of albumin may pass through the glomerular membrane, the blood pressure becomes elevated, and some edema exists. With regard to the latter point, it is interesting to note that in subsequent pregnancies there is either no edema or at the most a slighter degree than before.

It is well known that in a healthy person, under normal conditions, all of the glomeruli are not functioning at capacity at any one time, and it has been estimated that there is usually a margin of safety which approaches 50 per cent. In other words, there is a decided kidney reserve which may be called into play. It seems reasonable to suppose that in certain individuals this kidney reserve may be greatly decreased due either to congenital causes or to such factors as may have lessened the number of functioning glomeruli without producing a chronic nephritis. As we have seen in another group of cases, the strain of pregnancy always aggravates a chronic nephritis, so that later the kidneys are less well prepared to stand the strain of subsequent pregnancies. In the type of kidney under consideration this is not the case. All we can say is that the kidney reserve seems to be too low to meet the extra demands of pregnancy, as is manifested by the passage of a certain amount of albumin through the glomerular epithelium and by a moderate elevation of blood pressure, and that these manifestations usually disappear completely within two weeks after delivery. Furthermore, the kidney substance does not seem to have been injured by the pregnancy and the kidney reserve is certainly not lower for subsequent

pregnancies. Such kidneys appear to be quite capable of functioning adequately while the woman is not pregnant, as well as for her and her fetus up to about the eighth or ninth month of pregnancy, when manifestations of the low reserve begin to make their appearance.

Before presenting studies on cases of low reserve kidney, we should like to state that this term has been criticized on the basis that it is vague terminology and that placing responsibility upon the kidney primarily appears misleading and "to indicate a limited and faulty conception of a process having broader implications." Our conception of this group of patients may well be limited and faulty; however, we are just beginning to understand the intricate functions of the kidney, and are not even that far advanced in our knowledge regarding the etiology of certain types of hypertension. Volhard² stated "In the high pressure I see the cardinal problem of the entire renal pathology." There can be little doubt that the two factors mainly involved in hypertension are peripheral resistance and time-volume or cardiac force, and that of these the former is the more important, and may be due to not only an organic but also functional cause. One should bear in mind the fine blood pressure regulating mechanism of the organism. There is the powerful chemical regulation as well as the nervous one. It is conceivable that in what we have called low reserve kidney, the condition is more general, and the kidneys are not the important factor. However, it does not seem that, if it is a general, let us assume vascular, condition, the patient will, after conclusion of the involved pregnancy, proceed to have subsequent pregnancies during which there are no further or repeated signs of the general condition, that is, a reappearance of hypertension and albuminuria. It seems to us more logical to assume that the hypertension and albuminuria are dependent on a local kidney condition, which may not be present, at least to the same extent, in a subsequent pregnancy, or, if present to the same extent, the demands on the kidney in this subsequent pregnancy may be less or different. It seems, furthermore, logical to assume that even an essential hypertension, dependent upon arteriolar spasm, will not necessarily disappear after a pregnancy and what is even more important, not reappear in a subsequent pregnancy. The only other logical explanation, other than the assumption of such an entity as low reserve kidney, appears to be that in any given pregnancy there may be a substance or substances producing arteriolar spasm and so hypertension, but even then it is difficult to explain the albuminuria. However, in the light of our still incomplete knowledge of hypertensive disease as well as of kidney function, this may still be possible, and it is for that reason that we have stated above that our concept of the process involved may be limited and faulty.

Having admitted the inherent weakness in our argument and the possible pitfalls of such a limited concept as low reserve kidney to explain these cases, it seems to us that at present this is quibbling over

terms. It also is clear to us that this entity, as described above, has nothing in common with hypertensive vascular disease.

As albuminuria is a common finding in "low reserve kidney" patients, it is advisable that we consider some of the general aspects of proteinuria. Certain theories have been advanced to explain so-called "harmless albuminuria." Among these are lumbar lordosis, causing stasis of the renal veins, subnormal vascular development, and vasomotor instability. Elwyn⁸ states that in all types of albuminuria, with or without renal damage, there is either injury due to a poison or toxin, or anoxemia, that is, a deficiency of oxygen supply, but that in all cases there is damage to the glomerular and capsular epithelium. Discussing the type of albuminuria seen in supposedly healthy individuals, Thorp and Wakefield⁹ go so far as to say: "The burden of proof rests with those who do not consider it due to renal injury."

It is known that changes in the alkalinity of the blood can produce albuminuria, as it is found in acidosis, while alkali therapy decreases the amount of albuminuria. The albuminuria observed in nervous individuals may be due to localized areas of anoxemia, due to an instability of the vasomotor mechanism.

From these few general considerations of albuminuria, other than that accompanying definite and proven damage to the glomerulus or tubule or both, it would seem that this "harmless" albuminuria seen in low reserve kidney is most probably dependent on kidney changes per se, unless such general conditions as acidosis or vascular instability are the cause of it, and this latter assumption appears to us somewhat improbable as the condition is generally not accompanied by a nervous state or acidosis, and not even a more marked compensated alkali deficit than that seen in all normal pregnancies.¹⁰

We shall now consider 313 patients with low reserve kidney, who were admitted to the Lying-In Hospital during the period Sept. 1, 1932 to Dec. 31, 1933. We are not including any patients admitted after that period, in order that we may present a reasonably adequate follow-up study, as more than three years have elapsed since the last admission of the period studied.

TABLE I. INCIDENCE OF LOW RESERVE KIDNEY AND CHRONIC NEPHRITIS IN 3,352 FULL-TERM AND PREMATURE DELIVERIES

DIAGNOSIS	NO. OF CASES	INCIDENCE
Low reserve kidney	313	9.33%
Chronic nephritis	80	2.38%
Unclassified	58	1.73%

In 3,353 full-term and premature deliveries we find the number of low reserve kidney patients to be 313 or an incidence of about 9 per cent. In this group of patients there were no maternal deaths, while the incidence of infantile mortality was 5.91 per cent as compared with a clinic figure of 4.56 per cent, a difference of not much significance. It

should be stated that by "infantile mortality" we mean all deadborn or stillborn infants weighing over 1500 grams as well as those dying during the first two weeks following birth.

TABLE II. MATERNAL AND INFANTILE MORTALITY IN LOW RESERVE KIDNEY

MORTALITY	LOW RESERVE KIDNEY	TOTAL CLINIC DELIVERIES
Maternal	0	0.1 %
Infantile	5.91%	4.56%

The age incidence, as shown in Chart 1, is significant in that it is almost identical with the age incidence of the total hospital group

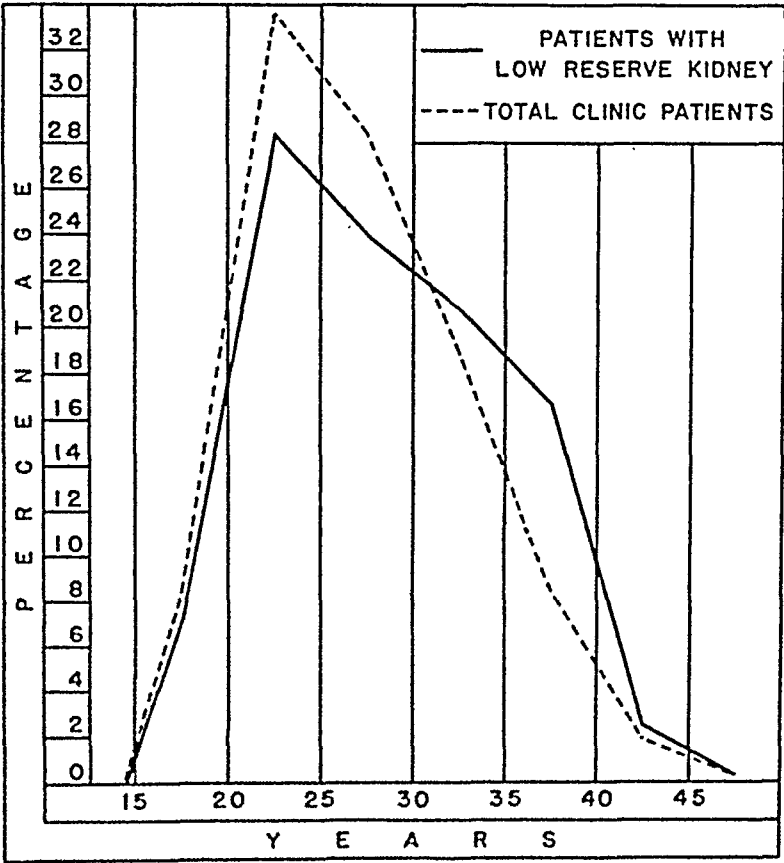


Chart 1.—Age incidence of low reserve kidney.

(clinic patients). There is no particular age group in which the incidence seems to be particularly high. When, however, this entity is considered in relation to parity we notice that it is a complication *particularly* of the first pregnancy. Chart 2 gives the parity incidence for 313 low reserve kidney cases, 80 chronic nephritides, and 2,619 nontoxemia patients in the group of 3,352 patients studied. We find that over half the cases of low reserve kidney occur in primiparas, whereas the clinic incidence of primiparas is only 45.8 per cent and that of chronic nephritis only 31.2 per cent. The curves in this chart are of further interest in that there is a marked relative increase in the cases of

chronic nephritis in subsequent pregnancies as compared with the total clinic, as well as the low reserve kidney parity incidence.

TABLE III. INCIDENCE OF COMPLICATIONS IN PATIENTS WITH LOW RESERVE KIDNEY

Complications:	PATIENTS WITH LOW RESERVE KIDNEY	TOTAL CLINIC PATIENTS
Cardiac disease	2.2%	3.07%
Pyelitis	1.5%	1.50%
Tuberculosis	0.3%	0.61%
Syphilis	1.2%	2.06%

Complications of pregnancy such as cardiac disease, pyelitis, tuberculosis, and syphilis apparently play no role in the etiology of low reserve kidney, as shown by Table III. Similarly, when we study previous

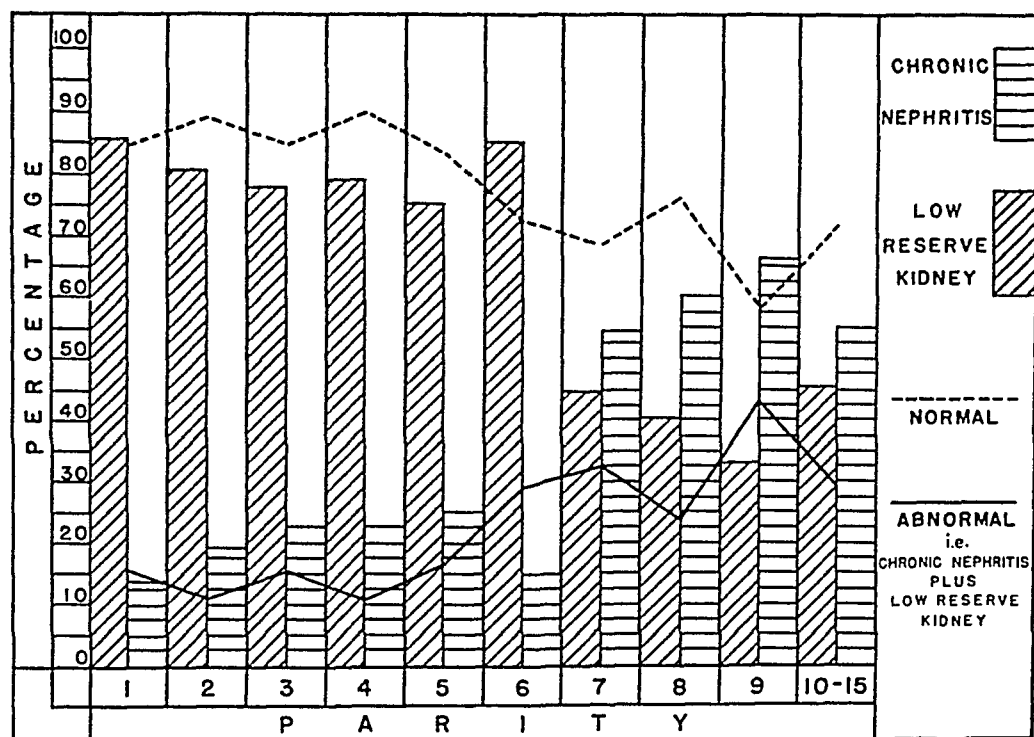


Chart 2.—Chronic nephritis and low reserve kidney in relation to parity.

diseases, as noted in the histories (Table IV), no correlation can be found between these and low reserve kidney, and this may also be said with regard to previous toxemia in an earlier pregnancy. Out of the total of 313 cases of low reserve kidney, only 14 had a history of toxemia in a previous pregnancy, 1 eclampsia, 4 chronic nephritis, and 9 high blood pressure, and it is extremely doubtful whether the previous diagnosis of chronic nephritis was correct as shown by Table V.

A study of the period of pregnancy at which the first sign of hypertension or albuminuria appears in these cases of low reserve kidney is of the utmost importance (Chart 3). It will be seen that the onset of these signs of low reserve kidney is mainly during the two last months of pregnancy, that is, from the thirty-second week to term. It never

TABLE IV. PREVIOUS DISEASE IN 313 PATIENTS WITH LOW RESERVE KIDNEY

PREVIOUS DISEASE	TOTAL CASES	NO FOLLOW-UP AFTER 1933 DELIVERY	AFTER ADEQUATE FOLLOW-UP	
			LOW RESERVE KIDNEY CORRECT DIAGNOSIS	LOW RESERVE KIDNEY NOW CORRECTED TO CHRONIC NEPHRITIS
Scarlet fever	25	13	12	0
Smallpox	1	1	-	-
Diphtheria	4	2	2	0
Typhoid fever	1	1	-	-
Chorea	2	-	2	0
Rheumatism	10	4	5	1
Nephritis	7	5	2	0
		26	23	1
Total	50	50		

TABLE V. PREVIOUS TOXEMIA IN 313 PATIENTS WITH LOW RESERVE KIDNEY

TOXEMIA DIAGNOSIS IN PREVIOUS PREGNANCIES	TOTAL CASES	NO FOLLOW-UP AFTER 1933 DELIVERY	AFTER ADEQUATE FOLLOW-UP	
			LOW RESERVE KIDNEY CORRECT DIAGNOSIS	LOW RESERVE KIDNEY NOW CORRECTED TO CHRONIC NEPHRITIS
Eclampsia	1	-	1	0
Nephritis, chronic	4	1	1	2
High blood pressure	9	3	4	2
		4	6	4
Total	14	14		

makes its appearance in the first half of pregnancy, and in this respect differs from chronic nephritis.

We now come to the most important part of this study, which is the behavior of the cases in subsequent pregnancies. Of the 313 patients with low reserve kidney diagnosis in a pregnancy during the period Sept. 1, 1932 to Dec. 31, 1933, we have 55 women returning to our hospital in a subsequent pregnancy. These 55 patients were carefully studied and a detailed "toxemia chart," similar to Chart 5, maintained for each. A survey of Chart 4 shows that of these 55 patients, who had the signs of a low reserve kidney in a previous pregnancy, 35 or 63.6 per cent, had no hypertension, no albuminuria, no edema and no symptoms indicative of toxemia, in the subsequent pregnancy. This observation, as we have said, is of the utmost significance. If this particular toxemia is dependent upon vascular changes, either organic (arteriosclerosis), nervous, constitutional (familial) or chemical in origin, one would suppose that all 55 patients should manifest at least such toxemic signs in a subsequent pregnancy, or perhaps those of actual kidney involvement (chronic nephritis of one or other type). The only other explanation for this striking observation, it seems to us, is that the original diagnosis of low reserve kidney should have been what Kellogg

calls preeclampsia Grade I. In this group of patients, however, we have at no time observed the other signs, symptoms and blood chemical changes described by Stander and Cadden¹¹ in 40 patients with preeclampsia. This, of course, may be partially explained on the basis of severity, and we are not prepared at present to state categorically that Kellogg's classification¹² is at error in this respect. Much further investigative work is needed before a final decision on this entity can be made. It is our present opinion, however, that from the clinical course, the behavior of the blood pressure and albuminuria, the blood chemistry

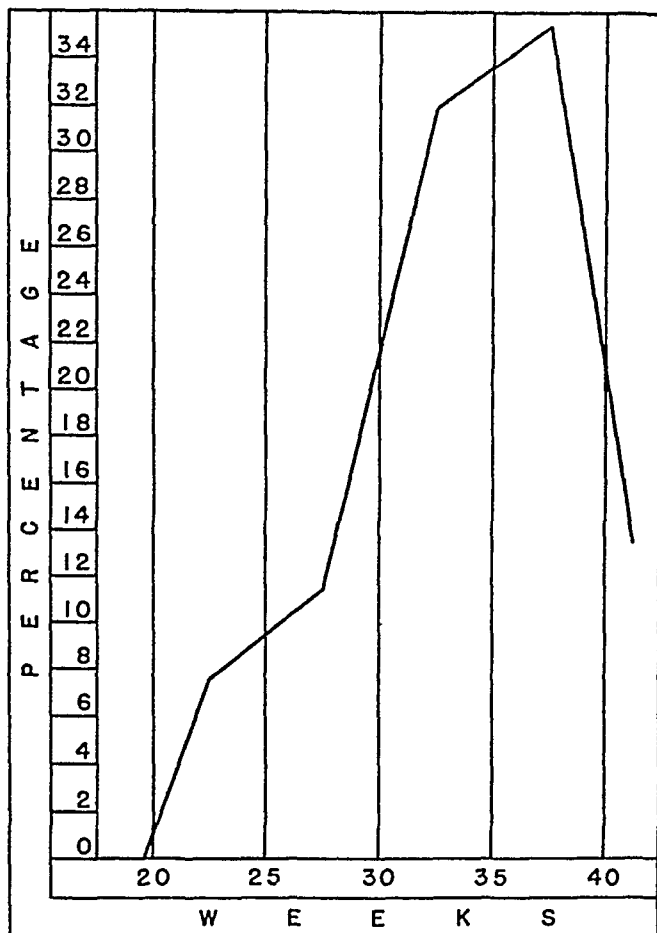


Chart 3.—Onset of toxemia in relation to duration of pregnancy in 313 cases of low reserve kidney.

and the eye-findings, the assumption of a low reserve kidney fits the picture better than that of a mild type of preeclampsia. Nevertheless, at present this is in great part only a difference in terminology, as the cause of the disease eclampsia, and its milder form, preeclampsia, is not yet known. But of the greatest importance, is the fact that this follow-up study in a subsequent pregnancy, indicates, and we believe, quite clearly, that the "low reserve kidney" findings cannot be explained on the basis of a general vascular disease with hypertension, as suggested by Herrick and Tillman.⁷

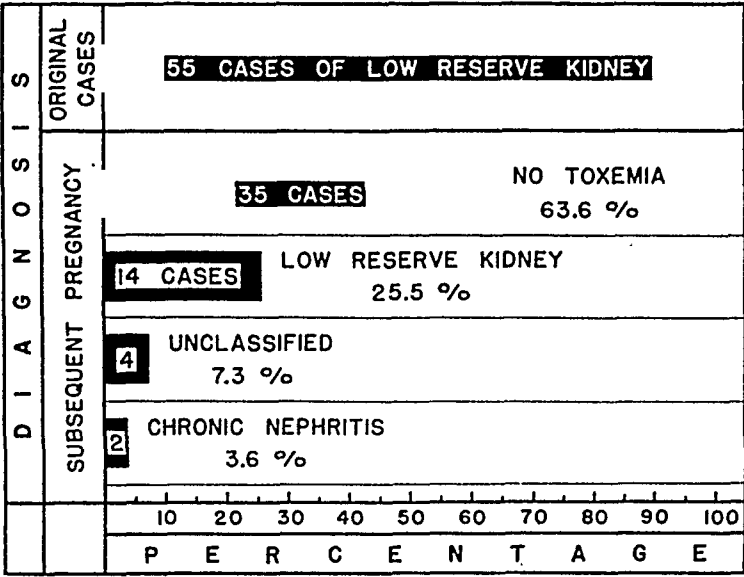


Chart 4.—Diagnosis in subsequent pregnancy in 55 cases of low reserve kidney.

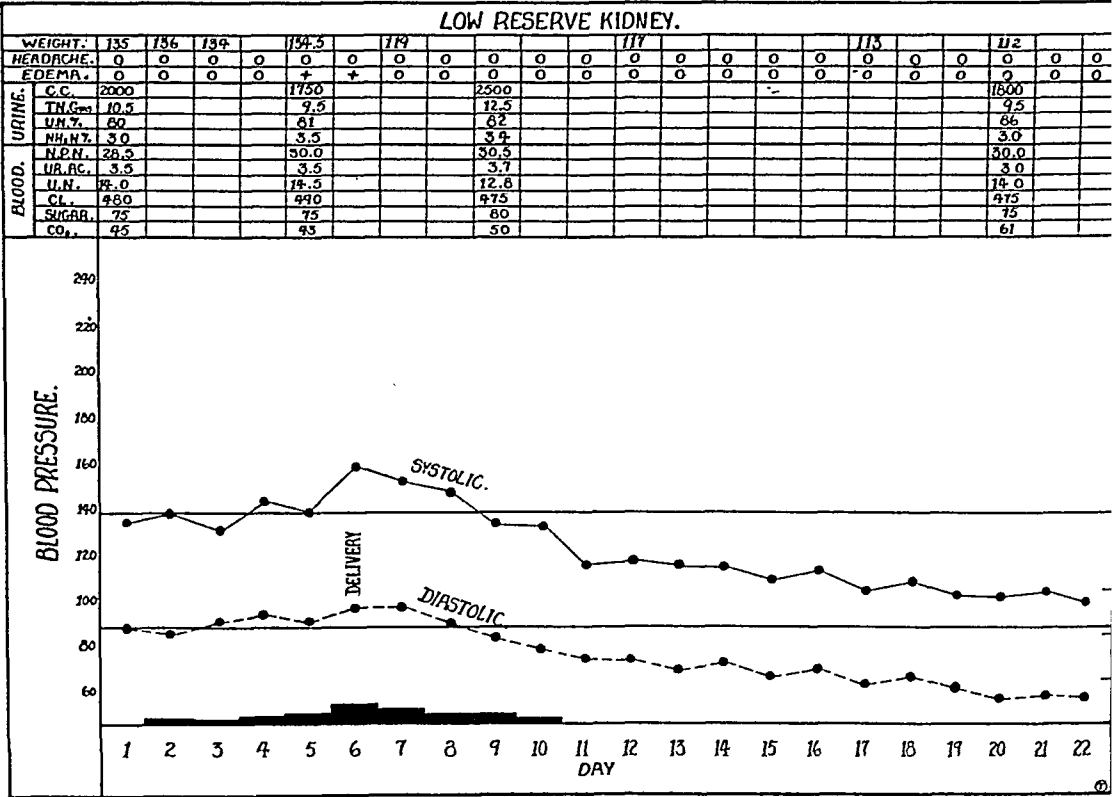


Chart 5.—Behavior of systolic and diastolic pressure, albuminuria and urine and blood chemistry in low reserve kidney. (From Stander, H. J.; *Williams Obstetrics*, New York, D. Appleton-Century Company, ed. 7, 1936.)

In Table VI is listed the treatment as to delivery, pursued in the original 313 cases of low reserve kidney. It will be seen that in no case was pregnancy terminated because of the toxemia, signifying a most conservative attitude, quite different from the one we follow in the treatment of chronic nephritis and to some extent of preeclampsia.

TABLE VI. TREATMENT IN LOW RESERVE KIDNEY

Type of Delivery:

Spontaneous deliveries - - - - - 228

OPERATIVE DELIVERIES	INDICATION		TOTAL
	FOR TOXEMIA	OTHER CAUSES	
Insertion of bougie for induction of labor	4		4
Cesarean section		11	11
Version and extraction		3	3
Breech extraction		9	9
Forceps	5	53	58
Grand total - - - - -			85

Incidence of operative deliveries = 27.15%

Total clinic incidence of operative deliveries = 21.95%

In the last table (VII) are listed 35 patients in whom we were unable to make a definite diagnosis during one pregnancy but were able to study these patients in a subsequent pregnancy. Of these 35 patients, 21, or 60 per cent, showed chronic nephritis in the subsequent pregnancy

TABLE VII. FINAL DIAGNOSIS IN GROUP OF 35 UNCLASSIFIED TOXEMIAS AFTER FOLLOW-UP STUDY

TOXEMIA	NUMBER OF CASES	INCIDENCE
Chronic nephritis	21	60.0%
Low reserve kidney	7	20.0%
No toxemia	2	5.7%
Remained unclassified	5	14.3%

and only 7 or 20 per cent, low reserve kidney. From this it may be concluded that we are too hesitant to make the diagnosis of chronic nephritis, and it would serve the patient's interest better if we were more rigid in the process of exclusion from the chronic nephritis group.

Finally, we wish to discuss briefly the diagnosis of "chronic nephritis." In the earlier part of this paper we mentioned the various types of nephritis and their respective etiologic factors. We are fully aware that many cases we group as "chronic nephritis" actually belong in the category of vascular hypertensive disease, without perhaps as yet actual kidney involvement. We purposely put them in the nephritic group, for the reason that we consider their condition far more serious than that of low reserve kidney, and that hypertensive disease, of whatever origin, either benign or malignant, sooner or later reveals kidney involvement, unless the patient succumbs from cardiac or apoplexy death before the signs of kidney involvement become apparent. From an

academic point of view it is well that we attempt, in each case falling in the large group "chronic nephritis," to establish the type of nephritis or the form of vascular disease, and this is done in every case in our hospital. Past history, clinical course, symptomatology, blood pressure, and albuminuria charts, repeated urea clearance, phenolsulphone-phthalein and dilution and concentration kidney function tests, microscopic examination of the urine, Addis' cell count, repeated blood and urine chemistry, repeated eye-ground examinations, and the observation of edema, are all of utmost importance in each case. We have so studied all our patients with signs or symptoms of toxemia, and have in many instances been able to diagnose the *type* of kidney or vascular involvement. However, from a practical standpoint we believe it is far more important to know whether the patient belongs in this general vascular-renal group, which we label "chronic nephritis" rather than to know the exact entity. We must know that the condition is not simply a low reserve kidney, or the more serious preeclampsia, but that it is a "chronic nephritis," as our treatment then is greatly altered.³ We would not interrupt a pregnancy for low reserve kidney, we would at times interrupt a pregnancy for preeclampsia, but we would never sterilize a patient in whom the diagnosis is preeclampsia, a procedure we often follow in chronic nephritis.

SUMMARY

We have presented a description of the present theories relating to the functions of the kidneys, and have attempted to indicate how these functions are affected in pathologic conditions. We have discussed the various types of nephritides, as well as general vascular conditions associated with hypertension and leading later to renal involvement.

A follow-up study of 313 patients with low reserve kidney is presented. The evidence, as revealed in subsequent pregnancies, strongly supports the concept of low reserve kidney and speaks against a general vascular disease or condition, whether of sclerotic, nervous, chemical, or familial origin, as the basis for this entity. Furthermore, it appears to be an entity distinct from any of the known nephritides, whether of the hemorrhagic, degenerative, or sclerotic type. It also does not seem to fall into the category of a mild preeclampsia. That this entity cannot very well be explained on the basis of a general vascular condition is the opinion, expressed in personal communications, of both Van Slyke and Marshall. The former has had an opportunity, in his nephritic service in the Rockefeller Institute Hospital to study various phases of hypertension and of the different forms of nephritis, while the latter has been responsible for an important part of our newer knowledge relating to the functions of the kidney. These investigators concur with us in the view that the concept of low reserve kidney appears to be sound. It must be

pointed out, however, that it is not our opinion that the existence of such an entity has been proved and much further investigative work, especially upon maximum excretion capacity, is needed before we can prove or disprove this theory. Richards and Landis have given us some very valuable suggestions along these lines and we hope, in the near future, to be able to follow these.

We believe that in this group of low reserve kidney patients, one or other of the factors influencing glomerular and perhaps also tubular function, may be involved. Such factors are rate of blood flow through the kidney, permeability of glomerular membrane as well as tubular walls, extent of filtration surface (glomerular), and perhaps also the effective filtration pressure. Unfortunately, very little is known as to the factors influencing tubular reabsorption, except the factor of time of contact of the glomerular filtrate with the tubular epithelium. That the involvement of one or other or combination of these factors, bringing about the signs of this entity (low reserve kidney), is dependent on inherent or inherited differences from the normal, or on a specific pregnancy condition such as hormonal or chemical or vegetative nervous, cannot at present be decided. Pressure on the renal veins or kidney pedicle, as suggested by Marshall, in a personal communication, should also be borne in mind as a cause of the albuminuria, although this may not explain the hypertension. We have discussed at some length the nervous reflex mechanism, as well as the other factors influencing blood flow through the kidney.

CONCLUSIONS

1. The concept of "low reserve kidney" indicates that the ability to meet ordinary excretory demands is retained, while competence to meet extraordinary demands is impaired.

2. Such decrease in reserve may result from a diminution in functional capacity or from actual structural change resulting in a decrease in the number of functioning units.

3. The concept of "low reserve kidney" appears to us to be sound from the viewpoint of kidney physiology as well as from that of clinical observation, although we fully realize that much further investigation is needed, before the existence of such an entity is either proved or disproved.

4. In approximately one-half of our cases of low reserve kidney there is no recurrence of hypertension or albuminuria in subsequent pregnancies.

5. We do not believe that the assumption of a general condition, such as hypertensive disease, or a general vascular disease of whatever origin, nervous, familial, sclerotic, chemical or hormonal, explains this group of low reserve kidney patients, as in such event, there should be a return

or continuation of the signs in all subsequent pregnancies. A temporary circulatory disturbance may conceivably account for the signs of low reserve kidney.

6. We are of the opinion that with our present inadequate knowledge of kidney physiology, as well as of hypertensive disease, the term "low reserve kidney," although perhaps not accurate as indicating the real etiology, best describes the group of patients under discussion, and, instead of being vague and narrow in that it focuses attention on the kidney, serves a useful purpose for this very reason. In this connection we have particularly in mind the recent work on so-called "harmless albuminuria," and think that, in the interest of the patient, attention should be directed to the kidney.

7. It cannot be clearly shown that low reserve kidney is not a very mild form of preeclampsia, although we believe the evidence, and particularly the blood chemistry, is against such an assumption.

8. Low reserve kidney is distinct and different from all the known nephritides, whether hemorrhagic, sclerotic or degenerative.

9. Low reserve kidney appears most frequently in the young woman with her *first* pregnancy, as shown by Peckham and Stout.¹³

10. Low reserve kidney appears only in the last month or two of pregnancy, and reveals itself by a mild hypertension and albuminuria and sometimes slight edema.

11. Kidney function tests and blood and urine constituents are normal in this condition.

12. The treatment for low reserve kidney is conservative as distinct from that in proved chronic nephritis.

13. The most common error in the diagnosis of low reserve kidney consists in designating cases of chronic nephritis or perhaps general vascular disease, as low reserve kidney. The incidence of low reserve kidney is, therefore, lower than we originally indicated, and accounts for probably only about one-third, or less, of all toxemias of pregnancy.

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LEUCOPLAKIA, LEUCOKERATOSIS, AND CARCINOMA OF THE CERVIX*

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A QUESTION which has been discussed repeatedly in the past few years is the relationship between leucoplakia and carcinoma. Does the leucoplakia of the cervix always, or at least in a significant number of cases undergo carcinomatous changes? A great deal of work, which can hardly be overlooked, has been done in attempting to answer this question. Frequently the problem is confused by the question as to whether the leucoplakia is not merely a precarcinomatous stage of the portio. The entire situation is thrown into further confusion by the improper use of the word "precancerous" or "precarcinomatous." Some authors use the word to describe pathologic changes which *invariably* lead to carcinoma while others use it to describe changes that *might* lead to carcinoma.

It must be pointed out emphatically that leucoplakia does not describe a definite and specific disease and that it presents neither a definite clinical entity, nor a well-defined pathologic, anatomic, or histologic picture. For this reason, Robert Meyer, in his contribution to *Henke-Lubarsch's Handbook* (7: No. 1) refused to accept the usage of "leucoplakia" in the pathologic-anatomic sense. The word "leucoplakia" does nothing but convey the optic impression which the examiner gets either with the naked eye, or by means of a colposcopic examination; it describes a bright white patch. However, various changes of the mucous membranes lead to the formation of similar white patches. It is impossible to determine with the naked eye, or even with magnifying instruments, the type of pathologic changes which underlie the leucoplakia. Structural changes of the mucous membranes cause a reflection of light, thus forming white spots. This is only one part of the pathologic change involved, one which can be recognized with the naked eye. A part of a pathologic process is called a symptom; the word leucoplakia is used to describe an optic impression, it is nonspecific and may occur in various diseases of the mucosa. There are symptoms which are specific for certain diseases and with the appearance of these symptoms a diagnosis is definitely established. Leucoplakia definitely does not belong to this group of symptoms. The question as to whether leucoplakia is malignant or not can only be understood properly if we consider all the various changes of the portio mucosa, which fall into the optical group of leucoplakia. Since we are confronted with various

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changes, the question cannot be answered unless we discuss in detail every process which is grouped under leucoplakia. In the literature there are cases of leucoplakia described which were already carcinomatous when first observed (Kolevajeve, Franquè, Hinselmann); cases of leucoplakia which developed into carcinoma after a long period of time (Geller, Esser, Labadie, Puccioni), and finally cases which never offered any proof of malignant degeneration even after years of close observation (Philipp and Schäfer, Rogge). These reports appear contradictory. The various observers have described different diseases which have only the external appearance in common. Observations can only be of value where an exact histologic description is given of the mucosal changes which led to the histopathologic diagnosis of leucoplakia. Where such microscopic descriptions are not given, the observations are of limited value because of the nonspecific character of leucoplakia as a symptom. "Leucoplakia" should no longer be used as a misnomer nor should there arise the question of "leucoplakia" degenerating into carcinoma. An analogous question would be: Can icterus develop into carcinoma? There are cases of icterus which have nothing in common with carcinoma formation, hemolytic icterus for example. Another group of icterus, the obstructive type, may lead secondarily to carcinoma. Finally icterus may develop as a symptom of carcinoma of the liver or gall-bladder. Icterus is neither a disease nor a diagnosis, but a symptom common to several diseases; its relationship to the development of carcinoma is manifold. The relationship between leucoplakia and carcinoma is similar. In order to avoid confusion and to understand properly the relationship between leucoplakia and carcinoma, we must discard the use of the word as a diagnosis and use it as a symptomatic description only; the diagnosis of the affection that appears as leucoplakia should be made on histologic findings only.

Clinically, the word leucoplakia does not convey a definite, characteristic picture. They vary in size, shade and may have a well, or poorly defined borderline. Some appear as white spots on the surface of a reddish portio and are easily recognized. There are various shades of leucoplakias, from the pure white to a shade slightly brighter than the surrounding mucosa, so that the color difference can only be discerned on close examination with optimal light. Leucoplakias may be set off from the surrounding area by a sharp, linear borderline or they may merge gradually into the surrounding darker area. Other characteristics which may or may not be present are: niveau differences, or a dull surface. These manifold differences between the various forms of leucoplakia can frequently be recognized with the naked eye, to say nothing about a colposcopic examination. On the other hand, leucoplakias which differ only slightly in color from the surrounding normal tissue may be easily overlooked during a hasty, routine examination.

In such cases iodine is very useful. Iodine application can serve to increase the number of clinically diagnosed leucoplakias by making visible the lesions which would otherwise escape the naked eye. Border-line cases, which cannot be or are hardly seen with the naked eye will be referred to as latent leucoplakias. The purpose of the iodine application is to make the grossly visible leucoplakia appear clearer and to make the latent leucoplakia visible to the naked eye. The iodine fulfills this function so well that the latent leucoplakia appears better defined and sharper than grossly visible areas of leucoplakia which were not treated with iodine. If there is a beginning carcinoma among the latent leucoplakia, the iodine will reveal its presence even if other clinical methods failed. Long clinical experience has shown that the number of latent leucoplakias diagnosed with the aid of iodine by far exceeds the number of grossly visible leucoplakias. Furthermore, all grossly visible leucoplakias are iodine negative, they appear as white, sharply-defined areas. On the other hand a large part of leucoplakias which can only be diagnosed with the aid of iodine are invisible to the naked eye. In this paper the word leucoplakia will be used to designate those mucosal changes of the portio which cause white patches to be visualized when aqueous Lugol's solution is applied. Normally the mucosa of the portio and vagina turns brown when Lugol's solution is applied, because of the glycogen content of the surface epithelium. In the absence of glycogen, there is no brown coloration. This may first of all happen when the normal, glycogen-containing epithelium is removed through trauma, as it may occur in the course of a gynecologic examination. These traumatized areas are identified by their sharp, ragged edges and by the partly attached traumatized surface epithelium. Their niveau is lower than that of the surrounding area. They appear as reddish white light spots when painted with Lugol's and regenerate within several days. The regenerating epithelium appears as an iodine-negative leucoplakia as long as it is glycogen free. These regenerative latent leucoplakias, which can only be seen after iodine application, have a smooth mirror-like surface and appear sunken in. Exact observation shows that they disappear in several days. The traumatic and regenerative leucoplakias do not lead to any permanent pathologic changes and are of no special interest here. The loss of glycogen-containing surface cells is due to extrinsic factors. The loss of glycogen-storing properties of the epithelium, as encountered in carcinoma and cornification, however, mostly is due to intrinsic factors. Cornification and carcinoma give rise to manifest, or latent leucoplakias. This observation proves that there are leucoplakias which are definitely carcinomas, or at least carcinoid or carcinomatous epithelium (Beläge). The exact nomenclature is neither of theoretical nor of practical importance. Leucoplakias, which show definite carcinomatous changes and fulfill all of Schottlander's and Kermauner's criteria for carcinom-

atous "Beläge" are admitted as "potential" carcinomas, even by observers who are diagnosing carcinoma by invasion only (Franqué, Freedmann, Ries, Rogge, Stone). If there is invasive growth in addition, then it will convince even the most critical observer of its malignancy. The only fact of importance is that the superficial carcinomatous layer, which sometimes resembles a leucoplakia, may retain its superficial character for months or years before becoming invasive. The answer to the question whether such leucoplakias can become malignant is that they *are* already malignant.

Cornification is another process which destroys the glycogen-storing properties of the portio epithelium. Thompson proposed to use the word leucoplakia for changes of epithelium only that are of the type of abnormal cornification. The ideally normal portio epithelium, as described by Hinselmann (Zentralbl. Gynäk. 57: 2402, 1933, Fig. 1); and by Schiller (Zentralbl. Gynäk. 57: 418, 1933, Fig. 2), contains in its surface layers, rhomboid, or flat cells. When stained with the usual acid stains, these cells show no protoplasm but empty chambers. Special staining with Best's alkaline karmin, or with iodine, reveals glycogen granules in these superficial cells. The glycogen content of these cells depends to a certain extent on endocrine secretions. It is regulated by folliculin; the glycogen content is increased during pregnancy, or in the premenstrual period. Folliculin, however, is not the only factor involved. Under otherwise normal circumstances there is sufficient glycogen in the portio epithelium of castrated or postclimacteric women.

Physiologically, the vaginal and portio epithelium remain at a level, which the normally cornified skin epithelium goes through in the course of its embryonic development. Up to the fifth fetal month the surface epithelium of skin contains glycogen granules; subsequently, cornification takes place, as Ciliacus pointed out, at first on the palm and sole. Vaginal, portio, and esophageal epithelium remain in the "glycogen-storing" stage, but the possibility of prosoplastic cornification is always present in these epithelia. Traces of cornification in the epithelium of the esophagus are not infrequent, as *Stieve* has shown. The portio epithelium always possess a latent potency for prosoplastic cornification. Adequate stimuli will awaken this latency. These stimuli may be external, such as constant pressure, dryness, or chronic inflammations; syphilis. Furthermore there may be areas which have a pathologic tendency toward cornification, without any known external or internal stimuli being present. In the field of skin ichthyosis there is a good example of this type of cornification.

The glycogen-storing epithelium of the portio appears transparent and has a smooth (mirror-like) surface. The cornified epithelium, however, appears opaque and bright because of the light reflection; the surface is dull and uneven because of desquamation of cornified cells.

The cornification and desquamation produce bright, sometimes even white patches against a darker background. In other words there is a typical picture of leucoplakia. Leucoplakias formed through cornification being different from the viewpoint of histopathology, from changes in epithelium through trauma or carcinomatous growths should be differentiated in terminology. This can be done easily by borrowing a term from laryngology where similar changes are called leucokeratosis (Fein, Identity of Leucokeratosis buccalis and laryngis, Monatschr. f. Ohrenheilk. 5: 37).

Cornification may be incomplete or complete. The former is characterized by the absence of a keratohyaline layer, the persistence of the horn-layer nuclei and is called *parakeratosis*. The latter is characterized by a keratohyaline layer and a completely hornified layer without cell nuclei; this is called *keratosis*. Excessive hornification is termed *hyperkeratosis*. Applying this terminology to analogous changes in the portio epithelium one may speak of leucoparakeratosis, leucokeratosis and leucohyperkeratosis. Leucohyperkeratosis is merely a higher degree of leucokeratosis and the division line between the two is more or less arbitrary. For the skin a certain degree of cornification is physiologic, so that one cannot regard keratosis of the skin as pathologic; a hyperkeratosis, however is pathologic.

Parakeratosis is an incomplete form of cornification. Throughout this paper the word leucokeratosis will be used to denote cornification in general and will be divided into two subgroups.

1. The incomplete cornification, or leucoparakeratosis; this is characterized by the absence of keratohyalin and presence of nuclei in the horn layer.

2. The complete cornification, in the case of the cervix it is an excessive cornification—leucohyperkeratosis. Here we have a keratohyaline layer but no nuclei in the horn layer. The leucohyperkeratosis develops from the leucoparakeratosis and nearly always has a marginal zone of leucoparakeratosis. The leucoparakeratosis develops from normal epithelium. It merges gradually from the normal, glycogen-containing epithelium; this gives it a blurred borderline when iodine is applied. Occasionally one finds leucokeratosis with sharp borderlines. On cross-section, however, these borderlines are perpendicular as contrasted with the oblique borderlines of carcinomatous layers. Histologically, there is an abrupt change in the type of epithelium; grossly there is a sharp linear border between white and brown coloration after iodine application. (Schauenstein, Arch. f. Gynäk. 85: 1908, Plate 15, Fig. 4; Hinselmann, Ztschr. f. Geburtsh. u. Gynäk. 94: 164, 1929, Fig. 1; Haselhorst, Ztschr. f. Geburtsh. u. Gynäk. 98: 1930, Fig. 5; Schiller, Arch. f. Gynäk. 133: 257, 1928, Figs. 3, 5, 16.)

The oft-repeated question whether leucoplakia of the portio is carcinomatous or precarcinomatous will not be understood properly unless it is divided into its two component parts. The first part of this question, whether the carcinomatous layers ("Beläge") are merely *precarcinomatous* or already carcinomas, is of little theoretical and of no practical value. The second part of the question is: are the leuco-

keratoses, which are not carcinomatous as yet, to be regarded as pre-carcinomatous in the sense that they *always* or only *occasionally* develop into carcinomas?

In answering this question it is advisable to classify leucokeratosis according to etiology. The syphilitic leucokeratosis is hardly worth mentioning because there are only a few cases encountered, not enough to draw any conclusions. Syphilis of the cervix is very rare and plays a small rôle in our material. There are only a few cases mentioned in the literature (l'Espérance, Haselhorst, Verdalle); among his 28 cases of leucoplakia, Kolegajev found one syphilitic only. Hinselmann reported only a few cases of syphilitic leucoplakias (Monatschr. f. Geburtsh. u. Gynäk. 77: 1927, Arch. f. Gynäk. 130: 212, 1927, Zentralbl. f. Gynäk. 52: 282, 1928). A few cases of syphilitic leucoplakias were reported by Gellhorn. In my series of cases, however, they were very rare. Over a period of many years I occasionally only found a leucoplakia in a patient with positive Wassermann test. The relative number of these cases is so small that it might have been a coincidence only to find a leucoplakia with a positive Wassermann. Definite causal relationship between the two could be proved by the disappearance of the leucoplakia and negative serology after antisymphilitic treatment. This actually happened in one of my cases, but one case is not conclusive.

The following is a report of two cases of leucohyperkeratosis with positive Wassermann, without descensus or prolapse.

CASE 1.—J. F., aged forty-one years. Menstruation began at sixteen, regular, every four weeks, lasting three or four days, last menstrual period three weeks ago. Patient complained of low back pain of three months' duration. This pain radiated to the left and was aggravated during menstruation. Gynecologic findings: Uterus about the size of a fist, irregular, hard, movable; adnexa and parametria negative. On the anterior portio lip there were several, small, fairly well-demarcated areas of leucoplakia. Posterior portio lip was badly eroded. Wassermann was positive. In view of the small fibroid and the patient's age, sterilization with x-ray was resorted to. Biopsy of a small wedge-shaped piece of tissue from the edge of a leucoplakic area showed fairly thickened epithelium, which changed from parakeratosis to typical hyperkeratosis with a wide, keratohyalin layer; the superficial, nuclei-free horn layer was nearly as thick as the rest of the epithelium. There was a marked, diffuse, inflammatory infiltration of the papillary bodies; this infiltration was also to be found where there was little or no cornification.

CASE 2.—P. Z., aged fifty years. Menstruation began at seventeen, every four weeks, profuse flow. One parturition, no abortions; pelvic inflammatory disease two years ago. Patient complained of severe pain of two weeks' duration, in the sacrum and left adnexa. Gynecologic findings: Uterus somewhat enlarged, not definitely made out, tenderness on motion; there was a small cervical polyp about the size of a pea presenting at the external os. Application of Lugol's revealed a sharply-defined leucoplakic area on the posterior lip. Microscopic examination showed extremely thickened and cornified epithelium. Patient refused treatment; follow-up examination ten months later showed no change in the leucoplakia. An interesting observation was that the surface of the leucoplakia was flat and did not follow the curve of the portio. Microscopic examination showed marked parakeratosis with beginning hyperkeratosis.

Does the leucokeratosis caused by dryness of prolapse tend to develop into carcinoma? This question can be answered by reviewing the incidence of carcinomas in cases with prolapsed uteri. In 1928 Höglér published his work on the relationship between carcinoma and prolapse, since then the observations of other workers appeared in the literature (Gunsett and Ritter, Heidler, Kraul, Boukalik, Tourneux, Natale, Emmerl and Taussig, Geller, etc.). The consensus of opinion is that the combination of carcinoma and prolapse is rather rare; a prolapsed uterus has less tendency to carcinomatous growth than a uterus in normal position. Indirectly, through secondary changes of the epithelium, the prolapse offers a certain degree of protection against carcinoma. It is certain that the highly differentiated, cornified and dried-out epithelium has less tendency toward malignant degeneration than the normal epithelium. Skin malignancy of the palm or sole is extremely rare in spite of progressed cornification and constant exposure

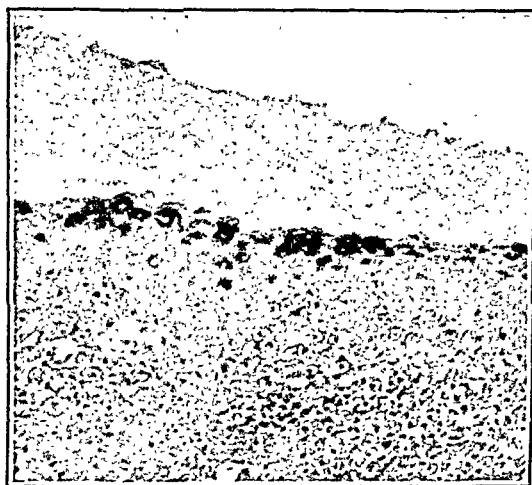


Fig. 1.—Syphilitic leucoplakia (Case 2); a well-developed keratohyalin layer with a thick superficial horn layer. ($\times 140$.)

to pressure of these two areas. On the other hand carcinomas of the skin are not rare where chronic irritation, arsenic poisoning for example, causes a hyperkeratosis. Neither the mechanical irritation, nor the cornification, as such, is of any significance in the development of carcinoma of the skin. The same observation holds true for the carcinoma of the cervix. The small percentage of carcinomas in prolapsed uteri with resulting cornification supports this observation.

Since neither the syphilitic leucoplakia, nor the leucoplakia caused by prolapse plays an important rôle in the etiology of portio carcinoma, we will pass on to a third group of leucoplakia, the spontaneous or autonomous type for which there is no apparent cause. This group of leucoplakia is of special interest because of its spontaneous character, comparative frequency, obscure etiology, and its possible causal relationship to carcinoma.

According to some authors the intermediate cornification, or the three-layer epithelium of the portio and vagina, is a result of premenstrual

changes. The author was able to show that this condition very frequently can be found independent of the menstrual cycle and occurs in postclimacteric as well as in castrated women. The epithelium next to the region of advanced carcinomas also shows this characteristic division into three layers. This epithelial change could be interpreted as a reaction to the carcinoma. It has been shown, however, that even the smallest beginning carcinomas originate in such a three-layer epithelium. In other words, the primary site of the carcinoma is prosoplastic, highly differentiated and has a predisposition to cornification prior to the beginning of carcinoma growth. The explanation to the apparent contradiction, between this statement and the foregoing conclusion concerning leucoplakia cornification in prolapsed uteri and carcinoma incidence, is to be found in the difference between the two types of cornification. The cornification in the prolapsed uterus is a physiologic reaction against drying. The cornification referred to as the third group, when occurring in a normally placed uterus, is a spontaneous, prosoplastic change; a sort of automatic hyperactivity of the epithelium, or due to the influence of hormone (folliculine).*

Vitamin-lack is the cause of a special type of cornification. It was recently discovered and was experimentally investigated in rats and mice (Evans, Reis and Perényi, Adler and Böttink, Wohlbach and Howe, Goldblatt and Benischek, Green and Mellanby, Euler and Mahnberg). It is a diffuse type of cornification and affects not only the vaginal mucosa but also that of the respiratory tract. In the animal it never causes a circumscribed cornification. The importance of this type of cornification in the human being is still unknown. It is possible that a local prosoplastic tendency to cornification is activated by a diet poor in vitamins. It is unlikely that there is any relationship between vitamin lack and the chronic leucoplakia of the portio, which even recurs after removal. In a recently published excellent paper, Swift demonstrated the relationship between achlorhydria on one side and hyperkeratosis and kraurosis of the vulva on the other side.

Do the more advanced types of cornification, as exemplified clinically by leucopara- and leucohyperkeratosis, also tend towards malignant degeneration? The reviewed literature does not answer this question satisfactorily. Cases of carcinomas developing from leucoplakia have been reported. However, the microscopic descriptions in all these cases either do not present exact histologic pictures of the leucoplakia or do not exclude the possibility of a primary carcinomatous surface epithelium. Only the case Alpers reported by Hinselmann serves to establish a relationship between carcinoma and noncarcinomatous leuco-

*According to Schwimmer, the leucoplakias of the mouth are caused by chronic inflammations (syphilis), or by chronic irritations (tobaccos, etc.). Brofeldt has the same point of view in regards to the leucoplakias of the mucosa of the lips. In an excellent work, recently published, Bencini has shown the autonomous character of the leucoplakia of the kidney pelvis.

plakia; but in this case there is no evidence that the area of leucoplakia primarily was a leucokeratosis.

According to the degree of cornification one can divide the leucokeratoses into two groups. In the first group the iodine test reveals extensive, confluent, irregularly shaped areas on the portio mucosa. These areas are brighter than the normal mucosa: they rarely appear white. Their colors generally range from dark yellow to light brown. Each area may have several shades. Microscopic examination shows slight parakeratosis with occasional remnants of glycogen-containing cells. Repeated examinations show that these areas of leucoplakia are very unstable. They disappear, sometimes within a few days and appear again with a different shade and outline. This type of areas of leucoplakia has no relationship with the portio carcinoma; it differs from the rare but stable carcinomatous leucoplakia by its flighty and inconstant character and its relative frequency as compared with the relative infrequency of portio carcinoma.

The second group consists of the true leucohyperkeratoses. It is distinctly apart from the syphilitic leucohyperkeratosis or the leucohyperkeratosis of prolapse. Clinical examination of the portio shows small, sharply outlined, white spots with linear borders and dull surfaces. Iodine application sets them off as bright, white spots from the surrounding, dark brown normal epithelium. These areas of leucoplakia examined with the naked eye greatly resemble the carcinomatous layers. Histologic examination shows definite hyperkeratosis with a typical keratohyaline layer and massive, nuclei-free horn platelets on the surface. Of special interest is the sharp, almost hair-like border between the area of leucohyperkeratosis and the normal epithelium. This sharp borderline is also characteristic of the carcinomatous layers, but here the borderline runs obliquely downwards, whereas in the areas of leucohyperkeratosis it is perpendicular. In the oblique carcinoma, demarcation lines are carcinoma cells in the basal layer and normal epithelium on the surface. The sharp straight but perpendicular borderline is characteristic of the hyperkeratosis. The oblique line of demarcation in carcinoma is the result of growth by assimilation in the basal layer; the shorter the time since the basal cells began their carcinomatous changes, the narrower the strip of carcinomatous cells which is regenerated by the basal cells. As a result, the thinnest layers of carcinomatous epithelium are to be found immediately over basal cells, which have undergone the most recent changes and vice versa. In this manner the oblique line is a sort of an indicator, pointing in the direction in which the carcinoma cells assimilate in the basal layer. In the hyperkeratotic leucoplakias the direction of the borderline is entirely different, it is just as sharp and linear, but always perpendicular to the basal layer; the line of demarcation between the two areas is at right angles to the surface. This finding can be explained by the

conclusion that these keratotic areas grow and extend toward, the periphery either very slowly or maybe not at all. In any case, with a sharp demarcation the straight course of the borderline is a regular and constant characteristic of this type of parakeratosis.

Close analysis of the changes involved in such an area of para- or hyperkeratosis will show the following:

1. The basal layer is the least affected. The cells are spindle shaped, have large nuclei and little protoplasm.

2. The prickle-cell layer is increased in thickness at the expense of the superficial layers. The thickness of the entire epithelium thus sometimes remains unchanged. In the normal epithelium the prickle-cells contain less protoplasm and show traces of glycogen as they approach the surface. In parakeratosis the prickle cells become more dense, homogeneous, and flat as they approach the surface. There is a gradual change so that the most superficial layers are composed of flat, homogeneous, dark-staining leaflets with almost black, shrunken nuclei in the center. Hyperkeratosis is merely a more advanced form of this differentiation. A keratohyalin layer is formed with a nuclei-free layer of hornified cells on the surface.

In leucokeratosis the stroma and papillary bodies show no changes whatsoever; signs of inflammatory infiltration are usually absent. In carcinomatous layers however, there is inflammatory infiltration of the stroma underlying the epithelium affected.

I had the opportunity to make clinical and histologic observations of a number of cases of leucokeratosis. Some of the cases have been followed for over five years. This group includes only cases which showed no evidence of syphilis, prolapse, or descensus. Search for signs or symptoms common to all the cases yielded very little. Thorough physical examinations, blood chemistry (cholesterol, etc.) and blood morphology also revealed nothing. As long as we cannot find characteristic general symptoms common to most of these cases we will have to regard this group of leucokeratosis as a result of local stimuli. These stimuli may be physiologic or pathologic.

Among a great number of leucoplakias, I found only nine cases of true leucohyperkeratosis without syphilis or prolapse. The ages of these patients ranged between twenty and forty; not one was postclimacteric. In older women, areas of leucokeratosis were always found to be associated with descensus or prolapse. Apparently the vaginal and portio epithelium loses so much of its reactive properties at menopause that a circumscribed local protoplasia can no longer occur. In none of these nine cases was there any evidence of beginning carcinoma. These areas of leucoplakia were unstable. Sketches made at each examination showed these bright spots with blurred borders changing their shades, outline, and location on the portio. Repeated histologic examinations showed that the parakeratosis never reached a high degree. The epithelium formed a superficial, thin, incompletely hornified layer with numerous nuclei remnants. Most of the cases described by Philipp and Schäfer probably belong to this group.

The transition to the rather small group of areas of leucohyperkeratosis is represented by a few cases. Here the areas of leucoplakia have sharply defined borders, a brighter appearance and are more stable from the point of view of development and localization. Colposcopic examination reveals, sometimes even without the use of iodine, small, bright, sharply defined spots, frequently slightly elevated. The following is a typical case:

CASE 3.—H. S., aged eighteen years. First menstruation at fourteen, irregular, every four to eight weeks, lasting eight or ten days. Patient complained of a four-month amenorrhea period and a loss of weight. Gynecologic findings: Normal sized uterus, anteverted, flexed, hard, movable; adnexa and parametria negative. On the anterior portio lip there was a small, oval-shaped, sharply defined, somewhat elevated area of leucoplakia. Histologically it consisted of thickened parakeratotic epithelium with beginning hyperkeratosis. In other words, it was a transition of leucoparakeratosis to leucohyperkeratosis (Fig. 2). Medical examination and

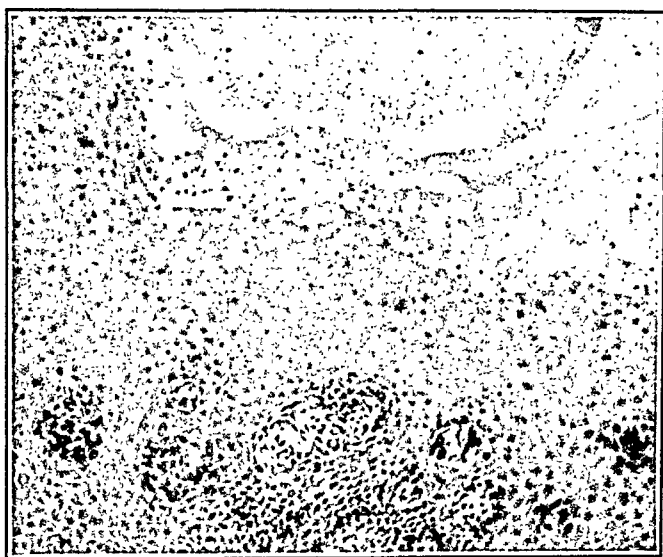


Fig. 2.—Case 3. Horizontal section, parakeratosis with a small patch of complete hornification; note the superficial layer without nuclei to the right of the midline. ($\times 140$.)

Wassermann were negative, blood chemistry was normal. Thorough follow-up for one year showed no changes in the clinical or histologic picture. After partial, and even complete removal of the area of leucoparakeratosis with a curette, it regenerated, identical in size and shape. This restitution, even after thorough removal, suggested that the cause for the prosoplastic changes of the epithelium was in the underlying stroma rather than in the epithelium itself.

Over a period of many years I found nine cases of genuine, spontaneous areas of leucohyperkeratosis. In four of these the uteri were extirpated for various other reasons so that we had the opportunity to study serial sections. Long clinical observations of these four cases were therefore impossible.

The following are typical cases of leucohyperkeratosis:

CASE 4.—M. N., aged forty-three years. Menstruation began at twelve, every four weeks, two or three days' duration, with cramps. Last menstrual

period five weeks ago. Patient never had sexual intercourse. She complained of a yellow fluor of one month's duration; this became bloody tinged lately. Gynecologic findings: One finger admitted with ease; uterus was of normal size, somewhat retroflexed, hard, and movable; parametria and adnexa negative; small cervical polyp protruding through the os; white vaginal discharge. During a curettage the uterus was perforated and was therefore extirpated. Histologic examination of the portio showed extensive areas of parakeratosis developing from three-layered epithelium with intermediate cornification. In one area the parakeratosis was replaced by an area of keratosis with a keratohyalin layer. In the basal layer there were edematous cells, the type which was sometimes found near beginning carcinomas* (Figs. 3 and 4).

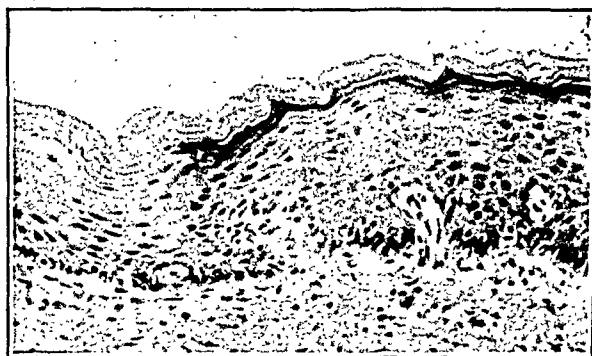


Fig. 3.—Case 4. Area of parakeratosis, left, and hyperkeratosis, right; note the sudden change and the vertical borderline between the two.

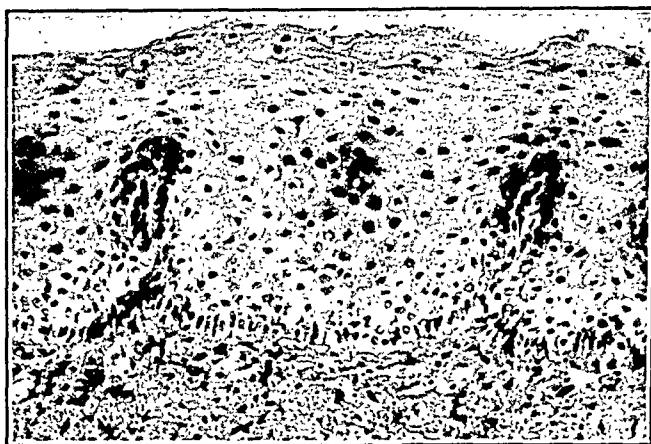


Fig. 4.—Case 4. Portio epithelium with parakeratosis; the cells of the basal layer are very edematous. (X5.)

This case deserves special attention because of the patient's virginity and negative Wassermann; external causes cannot explain the prosoplastic hornification. The cervical polyp was also no determining factor because cervical polyps are very seldom found together with hornified portio epithelium. It is probably a local process, comparable to the congenital hyperkeratosis of the skin.†

*Schiller: Arch. f. Gynäk., 130: 263, 1927, Fig. 18.

†I have examined three surgical specimens of uteri which were extirpated from virgins; one was from a forty-seven-year-old patient, extirpated because of adenomyoma; one was a corpus carcinoma from a fifty-two-year-old woman; and one was a fibroid from a forty-six-year-old woman. In none of the three cases was the portio epithelium of the ideal type, there were patches of parakeratosis, narrowing of the epithelium due to inflammation, etc. The most marked changes were in the case of adenomyoma where the epithelium formed irregular, pointed, and plump plugs. (Fig. 19A in Wien. med. Wchnschr. 36: 1172, 1931.)

CASE 5.—H. P., aged twenty-four years. Menstruation began at twelve years, every four weeks, lasting four or five days, regular until two months ago, para 0, gravida 0. Irregular vaginal bleeding and low back pain for past two months. Gynecologic findings: Normal sized uterus, hard, movable, anteverted, flexed; left ovarian cyst about the size of a walnut. On the anterior portio lip there was a small, bright, somewhat elevated area of leucoplakia with a dull surface and sharp borders. No other physical findings; Wassermann negative.

Histologic findings: A typical area of hyperkeratosis of the pavement epithelium with a well-developed keratohyalin layer and a wide, homogeneous nuclei-free horn

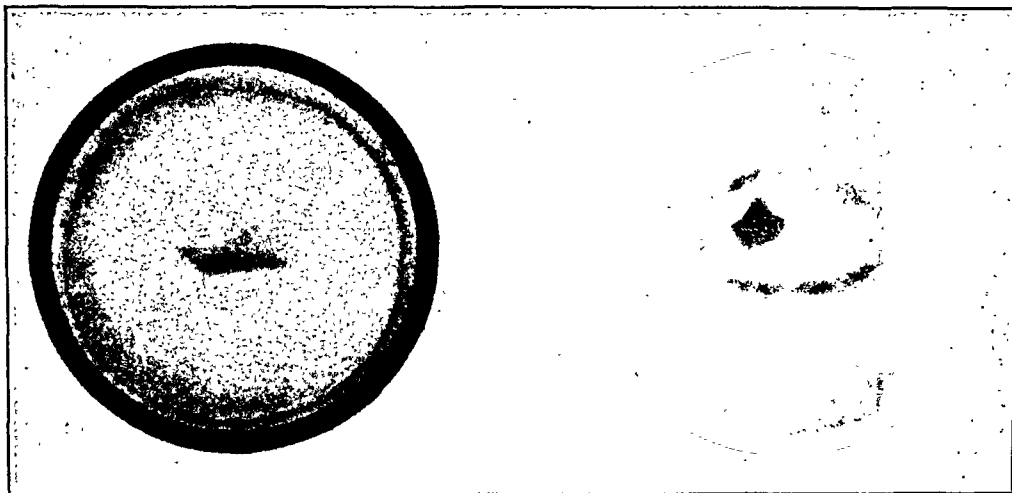


Fig. 5.—Case 5. (a) Cervix, a sharply defined bright leucoplakia to the right of the anterior lip. (b) Iodine application sets the lesion off as a white, sharply demarcated leucoplakia.

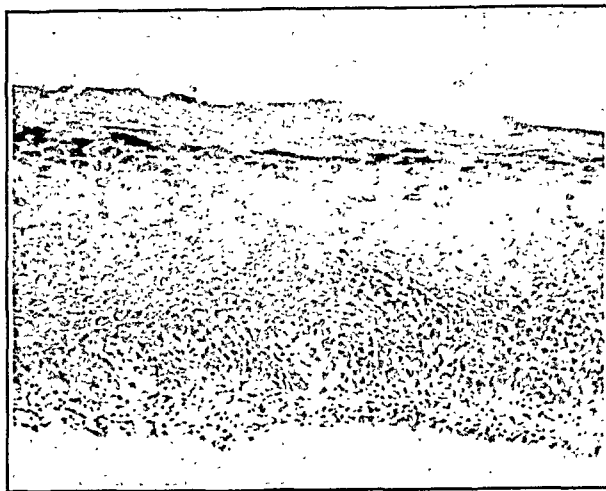


Fig. 6.—Case 5. Leucohyperkeratosis with cornified epithelium; well developed keratohyalin layer with a fairly thick, nuclei-free horn layer. ($\times 140$.)

layer. Close follow-up for over one year and a half showed neither gross nor microscopic changes. Repeated curettage of the lesion did not alter the picture (Figs. 5 and 6).

CASE 6.—G. G., aged thirty-three years. First menstruation at eighteen, irregular, every three or four weeks, lasting eight to twelve days. Sharp pain in the sacral region for some time; leucorrhea. Vaginal examination revealed no pathology. On the anterior lip there was an extensive, sharply defined, bright area which was histologically a typical leucohyperkeratosis.

CASE 7.—A. W., aged forty years. Menstruation began at thirteen, every four weeks, lasting three days. Nulliparous, six abortions. Wassermann negative. Patient complained of diffuse low abdominal pain and fluor of several weeks' duration. Vaginal examination negative. Iodine application and colposcopic examination revealed a more or less well-defined area of leucoplakia next to an erosion. Histologically it consisted of thickened, parakeratotic epithelium which occasionally



Fig. 7.—Case 9. Hyperkeratotic epithelium, distally from the external os, covering cystic cervical glands. ($\times 50$.)

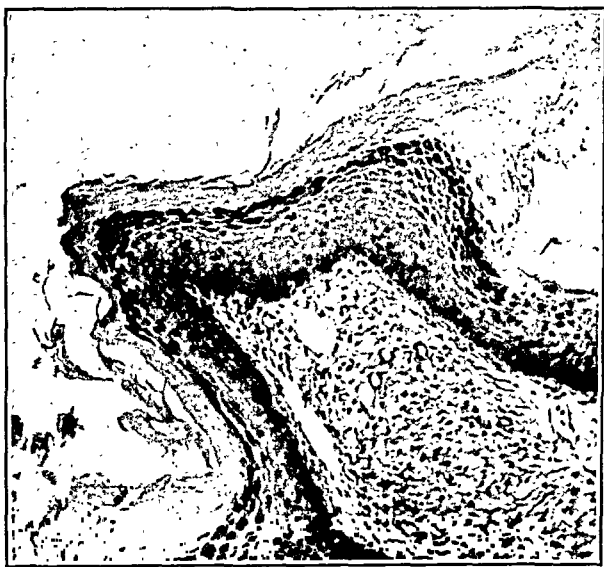


Fig. 8.—Case 9. Hyperkeratotic epithelium covering the space between two depressions that correspond to cervical glands. ($\times 140$.)

plugs erosion glands by means of plump cones. Some areas showed beginning cornification. Follow-up for several months showed slight regression of the areas of leucoplakia. The last examination showed areas of slight parakeratosis.

CASE 8.—M. W., aged forty-nine years. Menstruation began at sixteen, irregular, every four to eight weeks, lasting three or four days. Multipara, one abortion. Sacral pain of eight days' duration. Gynecologic findings: Uterus was plump, anteverted, markedly retroflexed; adnexa negative. Colposcopic examination showed

extensive areas of leucoplakia on both portio lips. Wassermann negative. Repeated examinations over one year showed no important clinical or microscopic changes. Occasionally the hyperkeratosis regressed to a parakeratosis.

CASE 9.—M. N., aged thirty-two years. Normal menstrual cycle since the age of eleven, gravida 0. Wassermann negative. Patient complained of vaginal discharge. Vaginal examination negative. On the posterior surface of the portio there was a white, sharply defined, wartlike lesion. Histologic examination revealed an advanced, true cornification area. In view of the extensive lesion and advanced pathology, the cervix was amputated. Examination of the amputated cervix showed an extensive, healing erosion, partly glandular and partly cystic. Most of the surface epithelium over the erosion was markedly cornified. The keratohyalin layer and the desquamating horn layer were fairly thick (Figs. 7, 8, and 9).

Notwithstanding long follow-up studies of numerous cases, I have never as yet found areas of leucoparakeratosis or leucohyperkeratosis developing into carcinoma. In 1928 I published the case of a forty-

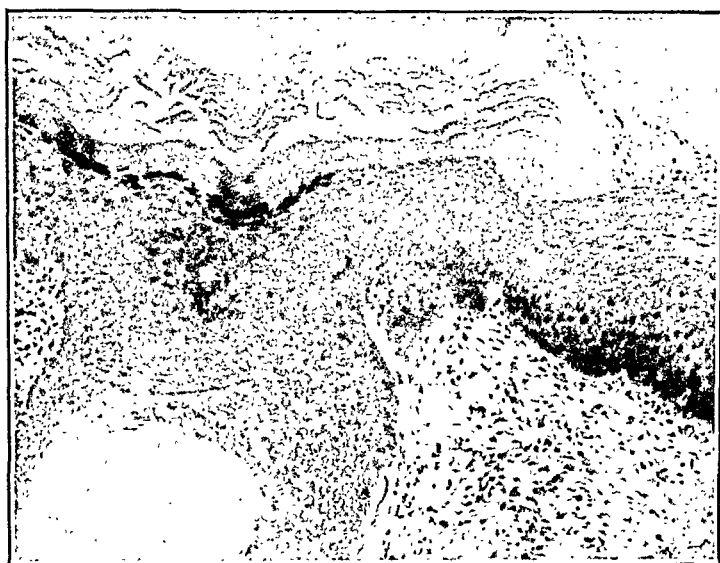


Fig. 9.—Case 9. Hyperkeratotic epithelium proliferating along a cervical gland, on the right a sharp vertical line of demarcation against the normal epithelium. ($\times 140$.)

four-year-old woman whose uterus was removed because of fibroids (Arch. f. Gynäk. 133: 253, 1928). I found an area of marked parakeratosis of the cervix which goes over in a carcinomatous layer. One exceptional case, however, is not sufficient to prove the relationship between areas of parakeratosis and carcinoma. Among many thousand cases I examined I found only one more case of a similar type:

CASE 10.—St. P., aged thirty-eight years. Menstruation began at twelve, normal cycle, regular until a short time ago. Para ii, one abortion followed by curetting. Patient complained of severe low back pains and dizzy spells. Examination revealed a fibroid uterus which was extirpated in the usual manner. The ovaries were found to have various-sized cysts.

Microscopic findings: The portio epithelium extended into the cervical canal. On the posterior lip, the epithelium, which contains islands of parakeratosis, very abruptly passed into a carcinomatous layer. On the anterior lip, the normal epithe-

lium very abruptly, under a sharp line of demarcation, changed into parakeratotic epithelium. In this parakeratotic zone, there was a small patch of normal epithelium sharply demarcated on both sides; it apparently corresponded to an *interlocking* between the normal and parakeratotic epithelium. About 6 mm. above the external os in the cervical canal, the parakeratotic epithelium directly passed into a carcinomatous layer ("Belag").

In this case the carcinomatous layer was covered, in certain areas, with a thin, easily recognizable layer of bright cylindrical cells. If one followed the cervical

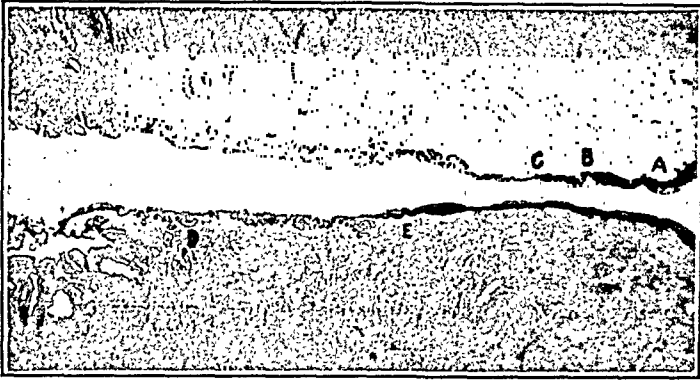


Fig. 10.—Case 10. Low power: Cervical canal, external os on the right. (A) The normal epithelium merging into parakeratotic epithelium. (B) A small plaque of normal epithelium within a parakeratotic zone. (C) Sharp, oblique borderline between normal epithelium and the carcinomatous layer. (D) Subcylindrical epithelium on the surface and around a cervical gland. (E) Carcinomatous layer and subcylindrical epithelium. (×6.)

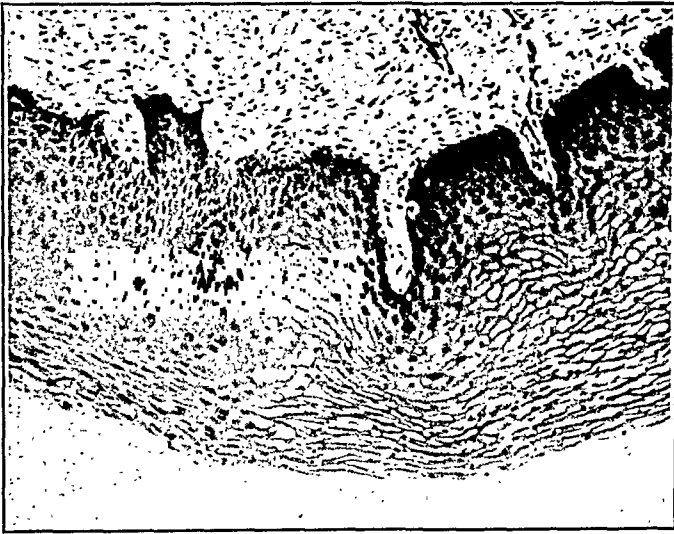


Fig. 11.—Case 10. (A, Fig. 10.) Normal epithelium right merging into parakeratotic epithelium, left. (×140.)

epithelium upward, one found partly ramified (*racemose*) glands and partly superficial cylindrical epithelium. As long as these cylindrical cells were an integral part of the superficial glands, or the superficial epithelium, they rested on one or more layers of solid cells. The deeper the cervical glands reached into the depth, toward the cervical wall, the less the number of subcylindrical cells encountered, and the less developed they were. The glands situated in the depth of the cervical wall had a normal appearance. Franqué investigated these so-called subcylindrical cells and Hinselmann described a typical case (Arch. f. Gynäk. 133: 64, 1928). Franqué does not regard these subcylindrical cells as the general origin of the glandular

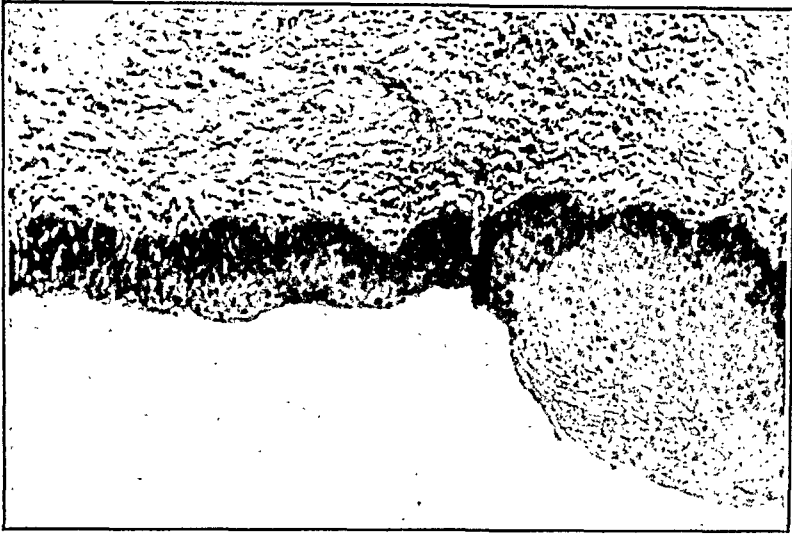


Fig. 12.—Case 10 (*C*, Fig. 10.) Oblique, sharp division line between the normal epithelium and the carcinomatous layer. ($\times 140$.)



Fig. 13.—Case 10. (*D*, Fig. 10.) Subcylindrical epithelium covering the surface and surrounding a cervical gland.

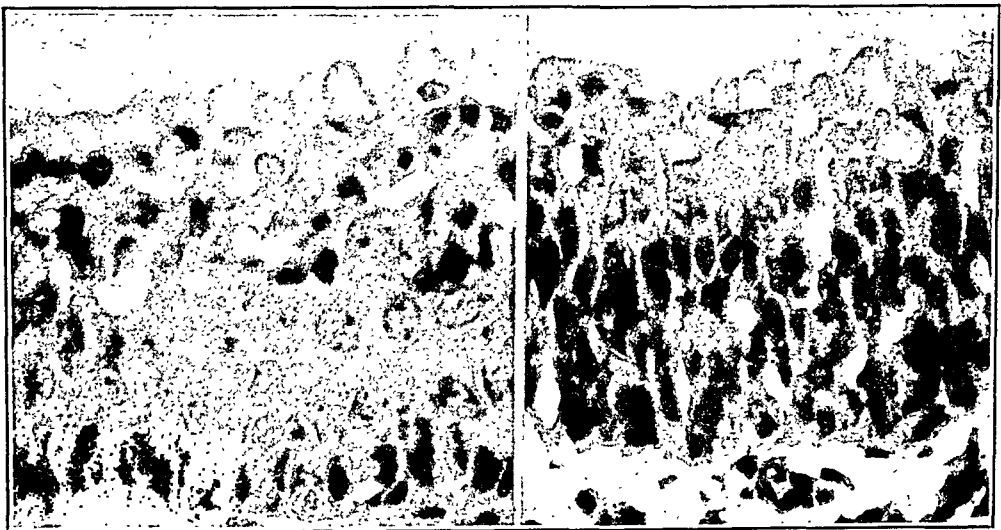


Fig. 14.—Case 10. (*E*, Fig. 10.) Showing carcinomatous layer functioning as subcylindrical epithelium. ($\times 800$.)

carcinomas of the cervix. In this particular case I have no doubt that the carcinoma developed from the subcylindrical cells. But it is a solid carcinoma and not an adenocarcinoma. Through this finding, that is, the development of the carcinoma from subcylindrical cells, this case loses an important point of analogy with the preceding case. Careful examination of serial sections did not reveal any subcylindrical cells in the cervical mucosa of the first case. In the first case the carcinomatous layer ("Beläge") developed from the portio epithelium; in the second case from subcylindrical cells of cervical epithelium, which was adjoining a sharply demarcated parakeratotic zone of the portio. Even if we were permitted to offer these two cases as proof that superficial carcinomas can develop from parakeratotic epithelium, the evidence would be worthless because of the numerous beginning carcinomas which develop without even the slightest trace of advanced parakeratosis in the adjacent areas (Figs. 10, 11, 12, 13, and 14).

There is no causal relationship between para- or hyperkeratosis and carcinoma of the portio. From extensive material I could not find even one case of carcinoma that developed from a true keratosis.* Cases with prolapse are excluded in this study; at best they disprove any relationship between carcinoma and cornification. In other parts of the body, mouth, lips for example, cornification plays an important rôle in the etiology of carcinoma. This was definitely proved by Schwimmer, Brofeldt, Ullman, etc.†

The situation with the portio epithelium is as follows:

The carcinoma develops from epithelium which frequently shows slight prosoplastic changes, as exemplified by intermediate, incomplete three-layered cornification. At best this prosoplastic change is a prerequisite and not a cause for the growth of carcinoma. This three-layered intermediate cornification is frequently nonspecific and not associated with carcinoma. Advanced cornification, even the autonomous form does not give rise to carcinoma.

These areas of leucoplakia do not warrant radical treatment, such as amputation of the portio advocated by some authors as a prophylaxis against possible malignancy. We found that these areas of leucoplakia remain for years without undergoing any changes. Malignant degeneration after ten or twenty years cannot be excluded, but our observations as well as those of Philipp and Schäfer point against it. If the histologic diagnosis is definitely established a periodic examination is sufficient. Radical therapy is not justified. These areas of leucoplakia are to be grouped with the benign hyperkeratosis of the skin rather than with the leucoplakic areas of the mucosa of the mouth or larynx.

The carcinomatous layer of the portio grows by assimilation of adjacent normal cells without passing through any intermediate stages.

*In the cases published by Esser, Franqué, Geller, Labadie, Puccioni and so on as carcinomas after leucoplakias, the leucoplakias probably have been carcinomatous surface epithelium and neither keratosis nor para- nor hyperkeratosis.

†According to Brofeldt about 25 per cent of leucoplakias of the lips degenerate into carcinomas. This does not hold true for portio epithelium.

This view is supported by the manner in which the carcinomatous epithelium passes into normal epithelium, the change is abrupt, without any areas of transition.

In the cornified carcinomas of the skin, however, the onset is gradual, and there is an area of transition from the normal to the diseased tissue. Between the normal and carcinomatous epithelium there is an intermediate zone which is not yet carcinomatous, and yet no more normal. Here the assimilation of the adjacent epithelium is slow and gradual, and apparently the beginning carcinoma also develops in a similar manner. As a result of this slow assimilation some times histologic pictures turn up which make a clear-cut classification impossible. As Delbanco first described it, the epithelium is in a state of restlessness, that is, the epithelium is no longer normal because of polymorphous cells and nuclei, on the other hand it has not reached the fully developed carcinomatous character as yet.

In the portio carcinoma there are no such transitions in the intermediate zone or before the beginning of the carcinoma proper. A suspicious appearing area of the portio when examined histologically will turn out to be either a leukokeratosis or a carcinomatous layer ("Belag"). The difference between the two is so marked that there is never a question of differential diagnosis.

Proliferations of the epithelium, however, due to chronic inflammation do cause confusion sometimes. This is especially true when one finds excessive production of immature cells in the basal and prickle-cell layers. Under such circumstances the differential diagnosis between excessive proliferation and carcinomatous layer is not simple. Among several hundred biopsies I found five cases of this type. These were followed up very closely.

The following are two of this group:

CASE 11.—H. K., aged forty years. First menstrual period at sixteen, every four weeks, four to six days, regular until two years ago, multiparous. Patient thought she was pregnant because of eleven weeks of amenorrhea. Gynecologic findings: Normal-sized uterus, anteflexed, hard, freely movable, left parametrium shortened somewhat; white vaginal discharge. Iodine application brought out, on the posterior lip, several pale patches with blurred borders. Biopsy showed marked thickening through parakeratosis, the nuclei of the deeper layers were somewhat polymorphous. The basal layer contained numerous mitotic figures. The rapid proliferation caused deformity of cells and entire cell groups. The prickle-cell layer was mature, with well-developed strands of epithelium. The surface layer was composed of partly glycogen-containing cells and partly of areas of parakeratosis. The mitotic figures here did not point to malignancy because they were neither atypical nor irregular. An increased number of *regular* mitotic figures was of no importance, especially during pregnancy.* In view of the few polymorphous and atypical cells, *excessive proliferation* was diagnosed. Repeated biopsies for a period of eight years failed to show malignancy. Occasionally the proliferation and parakeratosis diminished in intensity (Figs. 15 and 16).

*Vasiliu determined, statistically, the numerical relationship between mitotic and resting nuclei, without utilizing his results to practical advantage.

CASE 12.—A. S., aged thirty-seven years. First menstruation at sixteen, every five weeks, lasting three or four days. Two normal deliveries, one followed by chills and fever. For the past month patient had had irregular vaginal bleeding which was aggravated by contact. Wassermann negative. Gynecologic finding: Gaping vulva, old scar tissue in perineum and anterior vaginal wall. There was an erosion on

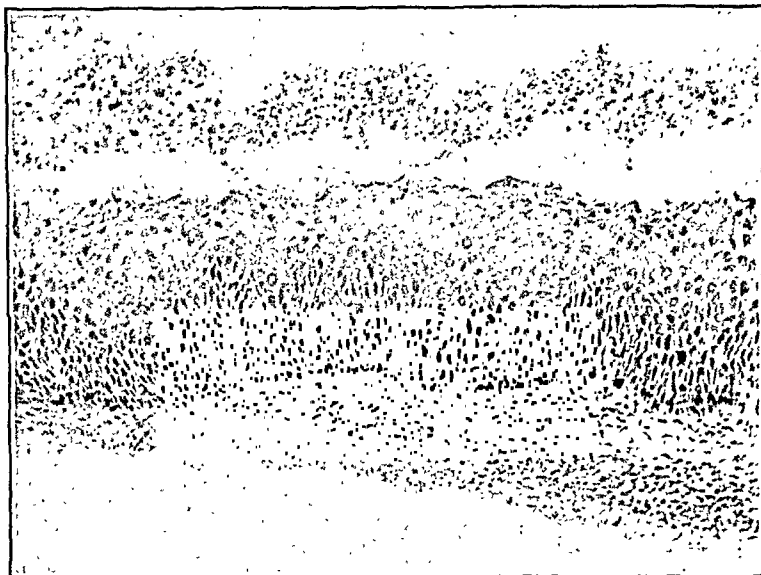


Fig. 15.—Case 11. Portio epithelium; the basal layer greatly increased in thickness at the expense of all other layers; frequent mitoses, the abnormal proliferation is causing crowding and deformation of the basal cells. ($\times 140$.)

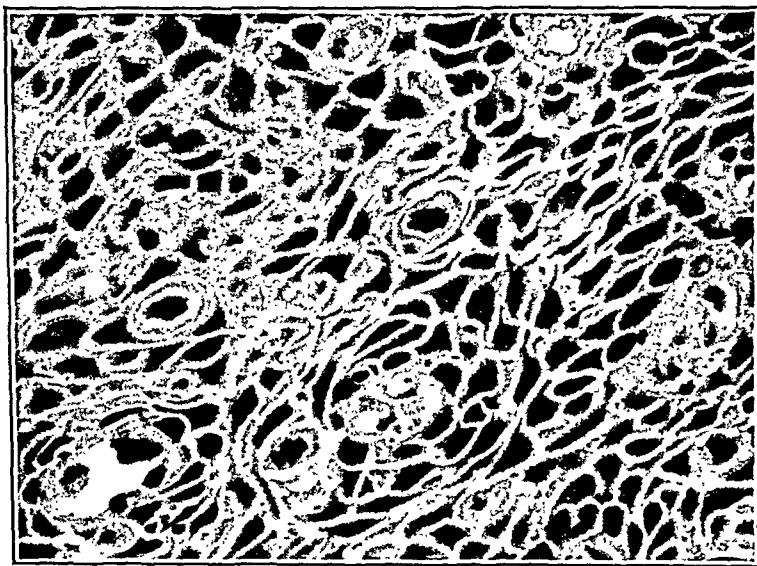


Fig. 16.—Case 11. Horizontal section through the basal layer; deformed nuclei, three typical mitoses, at the lower left a papilla and capillary cut transversely. ($\times 700$.)

the posterior lip. Iodine application left the erosion as a white patch. The posterior as well as the anterior lips had ragged craters with bleeding tissue at their bases. The edge of the erosion was composed of thickened epithelium, in a vascular network. The entire picture was that of an old, healing erosion. The squamous epithelium had a superficial, spongy glycogen-containing layer with areas of parakeratosis. The basal layer resembled the preceding case (Fig. 17); polymorphous or atypical

structures could not be found.* After four years the abnormal proliferation disappeared, but the parakeratosis increased somewhat in intensity. The gross appearance of the portio did not change.

These two cases are illustrations of abnormally rapid and excessive, but benign proliferation which may disappear in time. It is characterized by the accumulation of immature cells in the basal layer.

As in acanthosis the prickle-cell layer is increased in thickness in these cases, the basal layer is increased, which represents the *undifferentiated* zone or the *cambium* layer of epithelium. In these cases of pathologic proliferation, the mitoses are not confined to the basal layers only, they are also to be found in three or four cell layers overlying the basalis. This, however, is not due to an increased thickness of the basal layer which serves as an area of regeneration. As Thuringer pointed out, in



Fig. 17.—Case 12. Glycogen-containing, rapidly proliferating portio epithelium; most of the cells contain amitotic, double nuclei. ($\times 140$.)

the normal portio epithelium and in the squamous epithelium in general, mitosis in the prickle-cells immediately adjoining the basal layer is not uncommon. Nevertheless, in benign proliferation the epithelium above the basal layer reaches maturity, whereas in beginning carcinoma this is hardly true. The cause of such a benign proliferation is still unknown. We can offer an explanation only for a certain group of cases: During pregnancy there is a similar, but not such a marked change in the portio epithelium; there is a moderate increase in the thickness of the basal layer and in the number of mitotic figures. In these cases the proliferation is part of a general hypertrophy and hyperplasia of pregnancy. In cases without pregnancy endocrines may be responsible, thus drawing an analogy between this benign proliferation and the proliferation of the vaginal epithelium in rodents. This type of pro-

*In the prickle cell layer many cells show double nuclei.

liferation has nothing in common with malignant degeneration. As far as one may conclude from observations lasting for five to eight years, our cases of benign proliferation of the portio epithelium did not show the least tendency toward carcinomatous degeneration.

We still know very little about the precursors of portio carcinoma. Only in the negative sense can we draw several conclusions with a fair amount of certainty. According to Robert Meyer's, and my own investigations, neither erosions, nor inflammations form a basis for the development of carcinoma,* but even the leucokeratosis and the abnormal proliferation need not be regarded as precursors of portio carcinoma.

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JEWISH MEMORIAL HOSPITAL

*The Cancer Research Committee of the Marie Curie Hospital, London, Report of 1936, p. 36. It is generally believed that cervical lacerations and chronic cervicitis are important factors in the etiology of cervical cancer. There seems to be little evidence to support this view, and in our investigations of degree 1 and 2 cases—usually the only cases suitable for such an investigation—lacerations have seldom been found or when present may not have shown any relation to the cancer.

THECA CELL TUMORS

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IN A RECENT publication, one of us (S. H. G.) called attention to a group of tumors of the ovary, which because of their definite histologic, chemical, and biologic characteristics were considered to be related histogenetically to the theca interna cells of the ovary or their precursors. While this group has some histologic and clinical resemblance to the granulosa cell tumors, the morphologic features are distinctly different. The theca cell tumors simulate in appearance a fibromatous neoplasm. Because of this resemblance, and stimulated by the finding of three additional cases, we were prompted to review those tumors of the ovary which had been reported previously in the laboratories of the Mount Sinai Hospital as fibromas, or fibro- or spindle cell sarcomas. We were able to add three additional instances which we believe can be classified as of theca cell origin.

Histologic studies reveal various gradations from the cellular, malignant theca cell tumors to the more fibromatous types. It is conceivable that the fibromas and spindle cell sarcomas described by Robert Meyer as possible end-results of granulosa cell growth, and also some other tumors associated with feminizing influences may in reality belong to the group of theca cell tumors.

The clinical and morphologic characteristics of six additional cases of theca cell tumors are reported. Attention is called to their histologic variations and differential features. In the light of this investigation it is hoped that a sharper delineation of the theca cell tumors will be possible and their recognition and separation from the group of fibromatous ovarian tumors facilitated.

CASE 1.—Mrs. B. G. (P-3737, Courtesy of Dr. A. A. Berg) was admitted to the private pavilion of the Mount Sinai Hospital in December, 1929, because of left lower abdominal pain of several months' duration. She was fifty-five years of age, and aside from the fact that there had been no bleeding since her menopause, the history did not include any reference to somatic variations which might be interpreted as dependent upon abnormal hormonal changes.

Examination revealed the presence of a cystic mass in the region of the left adnexa. At operation a left ovarian tumor was removed. No notation was made at that time concerning the size of the uterus, nor was endometrial tissue obtained to determine a possible estrogenic effect of the ovarian neoplasm.

Pathologic Anatomy

Gross.—The specimen was approximately the size of a grapefruit, and cystic (Fig. 1). It replaced the ovary entirely and measured 15 by 12 by 11 cm. An intact

capsule encased the yellow tumor. The wall varied in thickness from 2.5 cm. at one pole, to paper thinness at the other. In the latter region there was evidence of hemorrhage into the wall. On section through the tumor it was found to be firm, fibrous and yellow. Grossly the tumor appeared to be an ovarian fibroma with cystic degeneration. The distinct yellow hue, however, and the rather cellular appearance suggested the possibility of a theca cell neoplasm.



Fig. 1.—Case 1. Cystic ovarian tumor with fibrous, yellow wall. Note thickness of wall at the right pole.

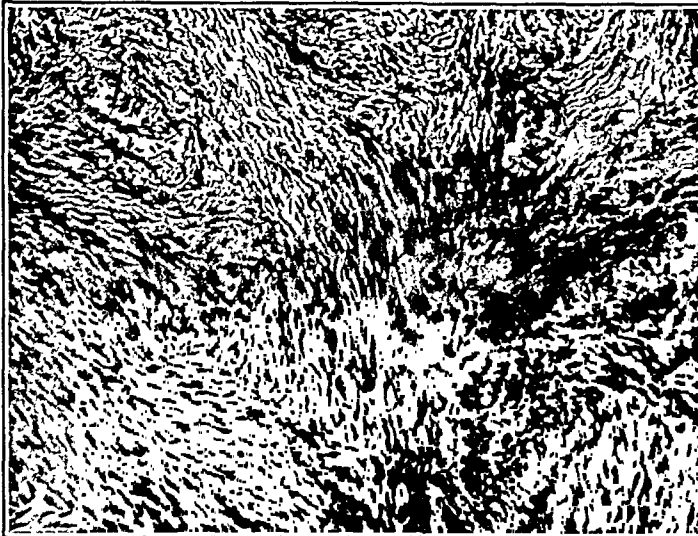


Fig. 2.—Case 1. Interlacing bundles of fusiform and epithelioid cells merging towards a hyalinized plaque.

Microscopic.—The histologic picture showed several characteristic features. The tumor was composed of interweaving bundles of closely packed cells cut in longitudinal and cross-section. Some areas were characterized by cells of a fusiform or spindle shape, but the more prominent type cell appeared polygonal or epithelioid, with a vesicular nucleus and a vacuolated cytoplasm. A delicate fibrillar arrangement of connective tissue separated the individual cells. Small hyaline plaques were numerous, and stood out prominently in the midst of the cellular bundles (Fig. 2).

From them fine fibers extended in a radial or tangential fashion into and about the surrounding epithelioid cells. The lipid stain demonstrated many minute sudanophilic droplets scattered within the cellular areas which were doubly refractile on polaroscopic study.

CASE 2.—The ovarian tumor described below was presented to us through the courtesy of Dr. William Anopol. Many of the clinical data were not obtainable, but the gross microscopic features were typical of a theca cell tumor. The patient was



Fig. 3.—Case 2. Yellow, lobulated tumor with white, fibrous septa.

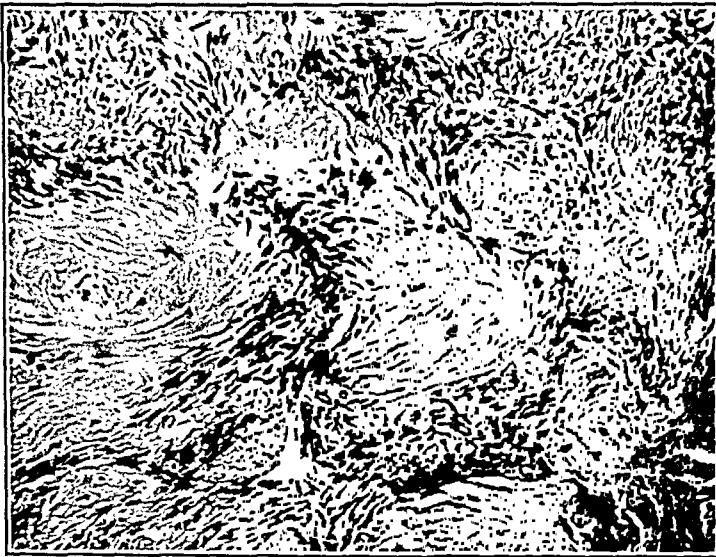


Fig. 4.—Case 2. Typical hyaline plaques with fibrous extensions into epithelioid cell groups.

a forty-six-year-old woman whose menses had always been irregular. Following amenorrhea of three months a period had occurred six weeks previous to admission. *Bleeding recurred and continued for two weeks before operation.*

Pathologic Anatomy

Gross.—The resected specimen consisted of a firm, nodular, solid ovarian tumor which measured 17 by 9 by 8 cm. (Fig. 3). Its surface was studded with numerous bosses of varying size. The ivory white capsule was complete throughout, but here

and there, the yellow color of the underlying tumor tissue could be seen. The neoplasm cut with a grating sound because of the abundance of fibrous tissue present. Cross-section showed a lobular structure. Thick strands of white fibrous tissue ramified throughout the tumor, separating numerous small and larger lobules of yellow cellular tissue. At one pole, there was an area of old hemorrhage.

Microscopic.—The characteristic features of irregular cellular strands separated by crescents or islands of acellular or hyalinized tissue was most conspicuous (Fig. 4). In the former areas the cells were closely packed and epithelioid in appearance. The nuclei were oval with blunted ends, or plump and spindle shaped, and rather vesicular. The azo-carmin stain emphasized the thin connective tissue fibrils which merged into the thicker collagenous fibers of the surrounding plaques. The yellow color was due to the large quantity of fat droplets within the cytoplasm of the cellular portion. A moderate quantity of these lipid particles were doubly refractile.

CASE 3.—(48219) G. F., sixteen years of age, was admitted to the gynecologic service in July, 1933. Her complaints included a primary amenorrhea and four months of lower abdominal discomfort. In addition, she had noted a tendency to hypertrichosis and a coarser quality to her voice over a period of four years. The general stature was feminine, but somewhat infantile, with a normally feminine shoulder-hip ratio. Her height was four feet, eight inches. The breasts were well developed for her age. Her voice seemed harsh. The fingers were short and thin and the joints showed excessive relaxation. There was some hirsuties, especially of the abdomen and the lower extremities. A slight mustache and long soft hair at the sides of the face were evident. The escutcheon was of the male type, and the clitoris was enlarged to 3 times the normal size, with definite overdevelopment of the prepuce. The hymen admitted one finger, and the vagina was somewhat contracted. The cervix appeared normal in size, sinistroversed and retrocessed. Posteriorly in the culdesac and to the right a hard irregular, freely movable mass the size of a small melon could be felt. At operation a bilateral salpingo-oophorectomy was performed.

Pathologic Anatomy

Gross.—The right ovary was replaced by a solid, firm tumor the size of an orange and measured 8 by 5 by 5.5 cm. (Fig. 5). The contour was oval and the surface smooth with an occasional irregular elevation. A complete capsule surrounded the gray yellow neoplasm. On section many small particles of calcified tissue were encountered by the knife. The tumor was divided by white fibrous septa into round or irregular yellow lobules. The individual lobulations presented a whorl-like appearance. The *left ovary* was enlarged to the size of a walnut and was similar in appearance to that of the right.

Microscopic.—The first microscopic section examined showed for the most part a typically fibromatous appearance, with wide strands of thick collagenous fibers, distributed in an irregular fashion. Further study, however, revealed many areas of different structure. These were moderately cellular and included broad bundles of basophilic epithelioid cells surrounded and encroached upon by partially hyalinized connective tissue strands. Many small plaques of calcification were present in the more fibrous portions. Fat stains and polaroscopic study showed the typical distribution of intracellular, doubly refractile lipid particles.

CASE 4.—(P-5239, Courtesy of Dr. A. A. Berg) B. P., a fifty-seven-year-old woman, was admitted in January, 1932, complaining of severe uterine bleeding, several years after the menopause. A large mass the size of a grapefruit could be felt in the

region of the left adnexa in addition to multiple fibromyomas of the uterus. At operation a supravaginal hysterectomy and left salpingo-oophorectomy and appendectomy were performed.

Pathologic Anatomy

Gross.—The resected uterus was enlarged to the size of a ten-weeks' gravidity by the presence of small intramural fibroids. It measured 10 by 7 by 5 cm. The



Fig. 5.—Case 3. Solid, yellow tumor lobules separated by white connective tissue septa.

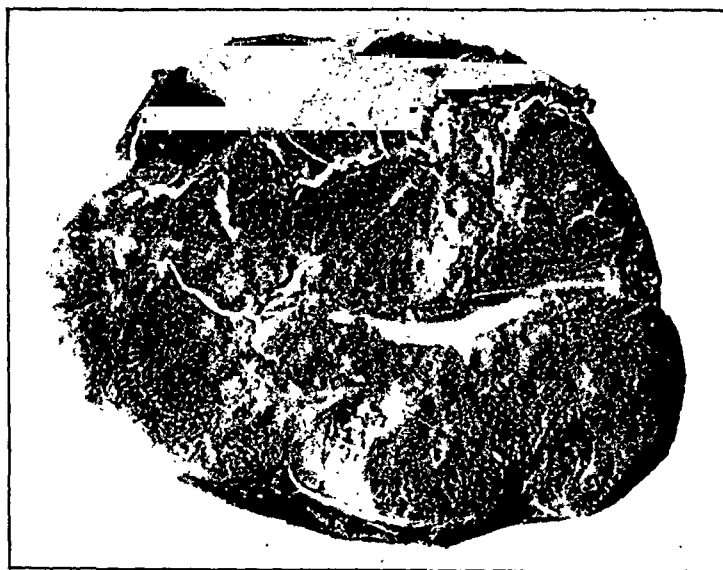


Fig. 6.—Case 4. Solid, encapsulated tumor with large yellow areas.

endometrium appeared hyperplastic and contained a small polyp in the region of the right horn. The left ovary was replaced by a solid ovarian tumor the size of a large orange, 12 by 8 by 8 cm. (Fig. 6). The surface was studded with numerous, small, firm nodules varying in color from ivory to yellow. The cut surface presented a lobulated structure. The strands of gray, fibrous connective tissue completely encapsulated the tumor, extending into it and separating the cellular yellow tan, bulging lobules.

Microscopic.—A marked cellularity was apparent on microscopic section, the tumor being composed of densely packed, plump, elongated spindle cells without any regularity of arrangement (Fig. 7). The nuclei of these cells were round or oval, large, pale and vesicular. Areas were to be found also in which the cell type was narrower and more fusiform, with slender, darker staining nuclei. Bundles of such cells especially when cut on cross-section suggested the appearance of smooth muscle tissue. At times at the periphery of some of the smaller lobules, very fine bands of

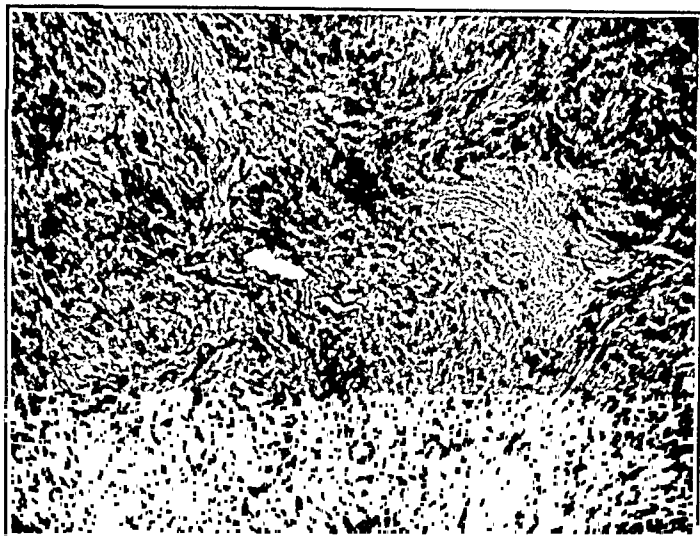


Fig. 7.—Case 4. Closely packed epithelioid cell bundles about a hyaline plaque.



Fig. 8.—Case 4. Markedly cellular tissue suggesting possible luteinization.

darkly staining, somewhat irregular and atypical cells could be seen. The tumor on the whole was vascular, containing both thin-walled capillaries and larger-sized vessels. There was some necrosis and hemorrhage present but not to a conspicuous degree. Hyalinization was not marked. The predominant type of cell was definitely epithelioid in character and closely packed, suggesting the structure of theca cells. Mallory stain demonstrated the distribution of fine fibrillar connective tissue between the cells. A moderate amount of cell atypism with nuclear variations and rare mitotic figures was noted. Though some of the cells could possibly be interpreted as re-

sembling granulosa cells (Fig. 8), no single area was found that in our opinion could be classified as a granulosa cell tumor tissue, not even of the atypical (spindle cell) variety. When stained with Sudan III an abundance of fine globules of fat was present. These included cholesterol or cholesterol esters as shown by their doubly refractile nature under polarized light. The uterine endometrium showed a hyperplastic appearance (Fig. 9).

CASE 5.—(P-10051, Courtesy of Dr. A. A. Berg, January, 1936). The patient was a forty-nine-year-old French cook who had never married. The menarche had begun at twelve, with regularly occurring periods every twenty-eight to twenty-nine days, lasting four to five days. The flow was moderately profuse. At the age of forty-six her menses began to decrease and become irregular. The menopause was complete one year later without further recurrence of bleeding. Eight months previously she had been hospitalized at another institution for eight weeks, supposedly for a bronchopneumonia involving the right lower lobe. The present complaints were of two and one-half months' duration and included swelling of the abdomen, a gain



Fig. 9.—Case 4. Hyperplastic endometrium, postmenopausal.

of twenty-two pounds in weight, constipation, occasional nausea and vomiting, anorexia and polydipsia. The temperature during the two days before operation ranged from 100.6° to 102° F. and the pulse from 112 to 120.

At operation two quarts of serosanguineous ascitic fluid were removed. A large irregular right ovarian tumor was found, with numerous adhesions to small and large bowel. Many small metastatic nodules were seen scattered throughout the peritoneal cavity especially in the broad ligament and posterior culdesac. The adhesions were separated and the tumor removed.

Pathologic Anatomy

Gross.—The neoplasm was a large, firm, irregular, oval shaped, yellow gray ovarian tumor, weighing 2375 gm. and measuring 21 by 20 by 14 cm. (Fig. 10). The surface was nodular. It was rather well encapsulated except for several small areas where the tumor tissue had perforated the capsule and appeared as small granular excrescences on the surface. Fibrous adhesions were present. On section the tumor could be divided roughly into two portions. One was composed of rather solid, medullary, cellular, grayish white tissue in which small, yellow areas were interspersed.

Here and there one could see small cystic zones and occasional hemorrhagic spots. The other portion was made up basically of hemorrhagic, degenerated, gray brown tissue containing large cavities lined by shaggy necrotic material. The lining of one small cavity was yellow and granular.

Microscopic.—The tumor appeared markedly cellular, with large areas of degeneration and hemorrhagic infiltration. Several portions looked sarcomatous, pre-



Fig. 10.—Case 5. Solid, degenerated, cellular tumor with perforated capsule. (Malignant.)

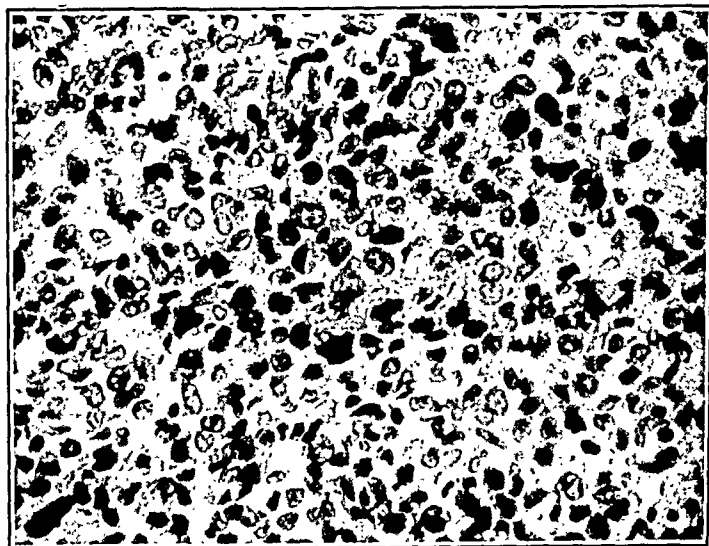


Fig. 11.—Case 5. Large, atypical, malignant, cellular areas.

sented conspicuous alterations in the cell and nuclear structure, mitoses, variability in staining reaction, and penetration through the surrounding capsule. The cells in these areas were not fusiform in shape, but rather epithelioid or round in appearance (Fig. 11). In the more benign, cellular portions irregular strands of plump, spindle cells interlaced in a haphazard fashion. Here numerous islands of polygonal cells with central nuclei were found. Fine fibrils extended between the individual cells and merged into the thicker connective tissue bundles which traversed

the entire tumor. Small hyaline plaques were scattered throughout (Fig. 12). In the substance of the tumor small glandular areas lined by high cuboidal epithelium could be seen which had a benign appearance and probably represented inclusion cysts from the peritoneal surface. This seemed especially evident in those sections showing nodular elevations of the tumor in close apposition. Frozen sections stained with Sudan III revealed numerous, fine fat droplets situated for the most part intracellularly and in cells which did not show any evidence of degeneration. Polaroscopic study showed the doubly refractile fat to be confined to the cellular areas and absent in the acellular or degenerated portions.

CASE 6.—(Courtesy of Dr. H. M. Rabinowitz and Dr. M. Jacobi, Beth El Hospital, Brooklyn, N. Y.) B. S., aged fifty-nine, was admitted to the Beth El Hospital in October, 1936, for postmenopausal bleeding. She had borne two living children and had experienced four spontaneous miscarriages and one ectopic pregnancy. On the latter account a left salpingo-oophorectomy had been performed twenty-five years before. Following her menopause at the age of fifty, the patient was well for six years. During the past three years, extending to the time of admission there had

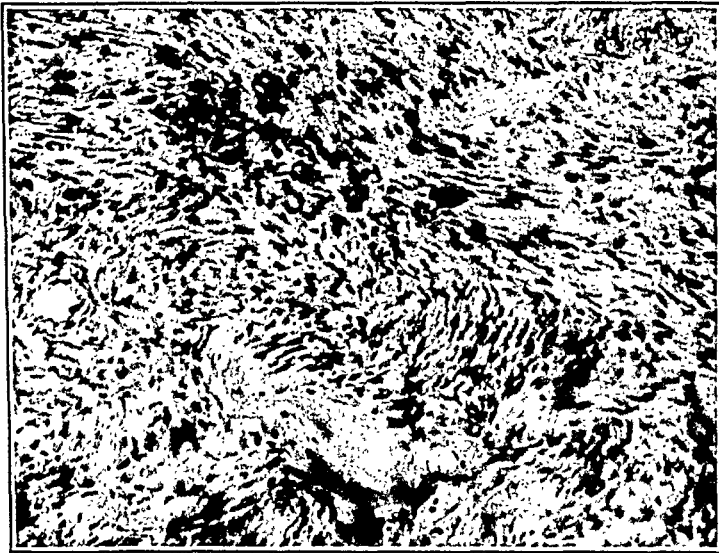


Fig. 12.—Case 5. Cellular but more regular spindle cell areas with hyaline plaque.

been intermittent vaginal bleeding of varying intensity, separated by periods of amenorrhea. Physical examination revealed the presence of a mild hypertension and a moderate secondary anemia. On pelvic examination the cervix was firm and lacerated, with active bleeding from its canal. The uterus was globular and enlarged to the size of a seven to eight-weeks' gravidity. In the right fornix, a hard, freely movable mass the size of a large walnut could be felt. A preliminary curettage showed polypoid hyperplastic endometrium. The presence of bleeding after the menopause, hyperplastic endometrium and a firm ovarian tumor pointed strongly to the diagnosis of ovarian, feminizing neoplasm which could be either a granulosa or theca cell tumor. A supravaginal hysterectomy and right salpingo-oophorectomy was therefore performed.

The resected uterus was enlarged approximately to the size of a seven-weeks' gravidity. It contained a few small, intramural fibroids varying from a pea to an almond in size. The serosa was smooth and the myometrium thickened to 3 cm. On section it presented a pink gray surface which was marked by the presence of numerous small areas containing old blood and an irregular arrangement of interlacing strands of fibromyomatous tissue. The gross picture was typical of adenomyosis.

The endometrial cavity measured 6.5 by 3 cm. Though much of the endometrium had been removed by a previous curettage, portions still showed a hyperplastic appearance. The fallopian tube was normal in size and configuration, although somewhat atrophic. The right ovary was replaced by a solid tumor, oval in shape and approximately the size of a small lemon. It measured 6 by 4 by 2.5 cm. The surface was irregular and nodular and its thin capsule intact. Its color was a mottled yellow white (Fig. 13). On section one portion seemed densely white and fibrous. Another was divided into lobules separated by white strands of irregular width. Some of the lobules presented a cellular, yellow tan appearance. Others were lighter in color and more fibrous, as though a greater concentration of thin



Fig. 13.—Case 6. Theca cell tumor (actual size).

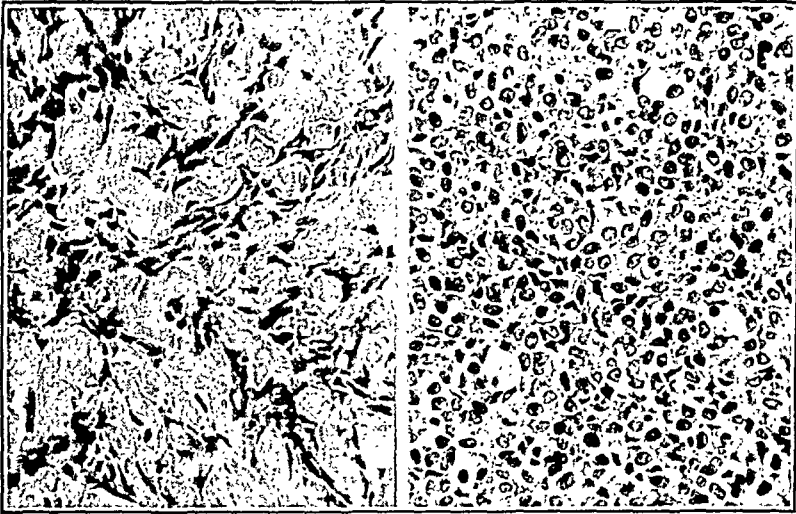


Fig. 14.—Case 6. Variations in the degree of cellularity within the same tumor.

fibers separated the cellular elements. One of the larger lobules measuring 1.75 by 1.25 cm. was cystic, the lining being covered by an irregular shaggy yellow tissue.

Histologic study proved unusually interesting because this ovarian neoplasm was illustrative of many variations encountered in different theca cell tumors (Fig. 14). Uniformity is not a constant feature of this type of tumor, the final picture depending upon the degree of cellularity, the tendency toward fibromatous and hyaline changes, degeneration and cyst formation. The areas seen as white and firm were found to be fibrous, but included numerous, markedly cellular strands. In many of these, among densely packed, oval-shaped cells, hyaline cords were conspicuous. The yellow lobules which stood out so prominently on gross examination were recognizable as conglomerations of large, epithelioid and oval cells. In some of them one could trace a gradual transition from the periphery inward; from the spindle to

epithelioid or oval cells, and finally to those which might be interpreted as theca lutein in appearance. The cells were for the most part oval or epithelioid, with vesicular nuclei and distinct nucleoli. The cytoplasm appeared foamy. Scattered, single, hyperchromatic nuclei were occasionally seen, and rarely, mitotic figures. Areas of degeneration and edema were not infrequent. The lipoid stain corroborated the expected, typical distribution of fine, intracellular, sudanophilic droplets, often not visualized except under high magnification. The uterine myometrium showed a marked adenomyosis. The endometrium was distinctly hyperplastic.

DISCUSSION

An analysis of the six cases described above together with those published in 1935 (5 cases) indicates that a definite classification of theca cell tumors is possible. The tumors may vary from moderately fibrous types to those showing marked cellularity or even malignant characteristics. To date, of the 22 cases reported in the literature only two were malignant; one described by Loeffler and Priesel and the other included in this paper. Genetically, the theca and granulosa cells have a common origin. In the course of neoplastic development either a pure theca or granulosa cell tumor may result. Because of their similar genesis, it is not inconceivable that a tumor containing both theca and granulosa cell tissue may occur.

The presence and distribution of fat within the theca cell tumors is of particular interest. It occurs far more extensively within the cellular islands than in the connective tissue framework. Polaroscopic examination reveals the lipoid to be doubly refractile, indicating the presence of cholesterol or cholesterol esters. Examination of fibromas, spindle cell fibrosarcomas and many other ovarian tumors failed to show this characteristic fat distribution, but the phenomenon was demonstrable in a granulosa cell tumor and to some extent in an arrhenoblastoma. Thus, of all the ovarian tumors studied only those possessing masculinizing or feminizing tendencies had this characteristic in common. We know, moreover, that the chemical structure of both the male and female sex hormone is closely related to cholesterol. It would seem therefore that within ovarian neoplasms a definite association exists between the presence of doubly refractile fat (cholesterol and cholesterol esters) and the tendency to induce sex changes. It is interesting to note that the dysgerminoma, a tumor which has no incretory function and does not affect the individual either in a masculine or feminine direction, fails to show intracellular fat.

Outside the ovary such lipoid storage may be seen in histiocytomas or xanthic fibromas of the skin, pseudoxanthomas and xanthomatoses or xanthic lipoidoses. These, however, are apparently manifestations of a reticulo-endothelial system response to a destructive or irritant process or to a disturbance in lipoid metabolism. As is well known some of these cases are associated with hypercholesterin-

emia. In one case of theca cell tumor recently published (S. H. G.) no disturbance of cholesterol metabolism was found. The question arose whether or not the cholesterol esters present in the theca cells were evidence of a histocytic function and whether theca cells possessed histocytic properties. Small quantities of lithium carmine (3 to 5 c.c.) were injected into the ear veins of virgin and parous rabbits at two-day intervals for a period of two weeks. The granulosa and theca cells of the well-preserved follicles remained free of carmine particles, as did the granulosa lutein and theca lutein cells. The carmine, however, was evident in large amounts within the plump, fat containing cells of the degenerating follicles or corpora lutea, and in an occasional cell within the ovarian parenchyma. The carmine containing cells were interpreted not as theca cells but as histocytes called forth as a response to the degenerative process affecting the follicle or corpus luteum. Neither the normal theca or granulosa cells apparently acted as histocytes.

We feel that we have been able to identify as a separate entity, a group of tumors whose clinical course includes not only those symptoms associated with any pelvic neoplasm, but also physiologic changes which are quite characteristic. These tumors most commonly occur in women past the menopause, though they have occasionally been found before the climacterium. Atypical bleeding is the most prominent symptom in the postmenopause cases, while metrorrhagia followed by a period of amenorrhea is frequently complained of in the younger women. There is often slight enlargement of the breasts and of the uterus. The endometrium presents a hyperplastic picture, resembling grossly and histologically that seen in other conditions presumably due to a hyperestrinemia. Operative removal of the tumors results in complete regression of symptoms. Geist and Spielman were able to demonstrate large amounts of estrogenic factor in a theca cell tumor. The tumor is usually benign but two cases have been described associated with ascites, and one with metastases, presenting all the clinical and pathologic evidences of malignancy.

Pathologic Anatomy

The theca cell tumors vary in size from that of a peach to neoplasms as large as a good sized melon. They are firm, irregular, solid or partially cystic. A fibromatous-like consistency and appearance is often suggested. A capsule is commonly present and is deficient only when tumor tissue, as in the malignant case described, has perforated it. The cut surface is distinctive; showing lobules of yellowish hue and varying size, separated by strands of fibrous tissue. Cysts, when present, may be small or almost completely replace the tumor, with occasional solid areas or thickened walls. The cysts result from degeneration and necrosis and contain cloudy yellow or hemorrhagic

fluid. The inner cyst wall sometimes has a shaggy appearance. Hemorrhage, necrosis and liquefaction may also be found in the solid portions of the neoplasms. An association with other pelvic tumors has been noted in some cases but no relationship can be drawn between the theca cell tumors and the uterine fibroids or ovarian cysts coincidentally found with them.

Histologically, the theca cell tumors represent a group that may closely resemble fibromas or spindle cell sarcomas, but have a decidedly characteristic histologic structure that distinguishes them from other tumors. The outstanding feature of their histologic composition is the presence of bundles of broad spindle cells, epithelioid in appearance, distributed in an irregular, interlacing manner throughout the tumor, separated by varying sized bands of connective tissue and often containing hyaline plaques. Fine fibrils traverse the intercellular spaces. The cells are usually regular in size, and the nuclei clear and well stained. At times they may appear to resemble luteinized cells. In the malignant type the usual evidences of cell atypism, nuclear variability and mitoses are to be seen. An important diagnostic point is the presence of doubly refractile fat in large amounts within the cells and to a lesser extent in the surrounding connective tissue. The lipoid is not degenerative in origin, but is stored or produced by the cells and probably is in some way related to the presence of an estrogenic hormone which has been demonstrated in the tumor and which presumed to be the important factor in the production of several of the clinical symptoms. The presence of large, fat containing cells, suggesting a resemblance to luteinized theca interna cells or granulosa lutein cells, was noted in the more cellular tumors in some instances.

SUMMARY

The anatomic and histologic characteristics of theca cell tumors are described, together with their distinctive clinical and hormonal features. Descriptions are given of six cases illustrating variations from the more benign fibroma type to the highly cellular and malignant type. A correlation is made between the presence of hormonal changes and the presence of intracellular, doubly refractile fat containing cholesterol and cholesterol esters. It is suggested that some of the ovarian neoplasms previously diagnosed as fibromas or fibrosarcomas may on further investigation prove to be of theca cell origin.

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100 EAST SEVENTY-FOURTH STREET

17 EAST NINETY-SIXTH STREET

DISEASE OF THE SPINAL CORD IN PREGNANCY

MYELOPATHY OF PREGNANCY, A CLINICOPATHOLOGIC STUDY

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THE clinical aspects of spinal cord disease of pregnancy have been well defined; however, the pathogenesis of the condition remains obscure. This obscurity is shared by many other complications of pregnancy, clues to the origin of which are lacking. The ultimate solution of the problem waits upon a more complete knowledge of the changes occurring in the organism during pregnancy in disorders usually ascribed to toxemia. Whether the disturbance is metabolic or endocrinologic, or due to some other factor, is at present not determined. Pending the time when such information will have become available, however, pathologic studies of the end-results of these complications of pregnancy may throw some light on the nature of the original disturbance. Pathologic studies of spinal cord disease of pregnancy have been recorded in a very limited number of instances. A number of these cases were reported as "myelitis" of pregnancy. The term, "myelitis," should be used to denote only such lesions of the spinal cord which are truly infectious in origin. As our and the other cases described in the literature are not true instances of "myelitis," we believe that the term, "myelopathy," is more appropriate.

REPORT OF CASES

CASE 1.—R. L., aged twenty-six, was admitted to the Montefiore Hospital in November, 1931. At the age of twelve she had developed an osteomyelitis of the right femur with recurrence at the same site when she was twenty-one years of age.

She remained well until August, 1930, at which time she was in the eighth month of her first pregnancy. The day preceding the onset of the illness, she had a slight cold which cleared up within twenty-four hours. The illness was ushered in by pains in the region of the back. A constricting sensation about the abdomen appeared about a week later and then there was difficulty in walking. In a few days she was unable to move her lower limbs. Following this, there occurred loss of sensation in the lower limbs and fecal and urinary incontinence. A cesarean section was performed and the patient was delivered of a normal child.

In November, 1930, the patient was observed at a neurologic hospital in New York City. The neurologic examination at that time showed a spastic paraplegia, with absent abdominal reflexes and a bilateral Babinski toe sign. There was a sensory level at the sixth dorsal segment with complete loss of all forms of sensation below that region. The cranial nerves were negative, except for a poorly sustained nystagmus on left conjugate gaze. Lumbar puncture did not disclose any evidence of a block. The spinal fluid was negative in all respects. Roentgen examination of the spine proved negative.

While the case was considered most likely one of myelopathy of pregnancy, the possibility of an osteomyelitis of the vertebrae was entertained and a laminectomy performed. At operation an atrophic cord, covered by engorged and tortuous vessels, was exposed.

Shortly thereafter the patient was transferred to the Montefiore Hospital. During the next few years of her stay at the hospital the condition of the patient became progressively worse. Examination performed in January, 1934, disclosed the following: The patient was bedridden, suffering from cystitis and from a large bed sore over the left hip joint. She was incontinent of urine and feces. Spontaneous movements of one limb or of both were occasionally noted. A flaccid paraplegia was present, with loss of all the deep reflexes in the lower limbs except the left ankle jerk and both adductor reflexes. The abdominal reflexes were present, but were diminished. The Babinski toe sign was present bilaterally. There was a sensory level at the sixth dorsal dermatome; below this point all forms of sensation were absent. Nystagmus was present on gaze to either side.

In March, 1934, the patient developed meningeal signs. Examination of the spinal fluid disclosed the presence of gram-positive and gram-negative bacilli and other findings indicative of a purulent meningitis. The patient died a day later.

Autopsy.—Gross Examination: Only the spinal cord was removed. The patient had a large decubitus ulcer about six inches in diameter involving the buttocks and sacrum. There was a fistulous communication between this ulcerated area and the subarachnoid space through which a probe could be passed. On applying pressure over the ulcerated area, pus was seen to enter the subarachnoid space.

The spinal cord was considerably swollen. The dura was slightly thickened; the pia-arachnoid, thickened to a greater degree, was adherent to the dura. On cutting the cord, the posterior columns in the cervical region appeared translucent. In the upper dorsal region the gray matter around the central canal was discolored. At about the third and fourth dorsal segments there was an area of reddish discoloration in the region of the posterior portion of the gray matter and the ventral portion of the posterior columns. At about the fifth dorsal segment, because of the hemorrhagic appearance of the cord, the outlines of the fiber tracts were obliterated. This reddish discoloration, which extended from the fourth to the seventh dorsal segment, was most intense at the sixth dorsal segment.

Various sections of the spinal cord at this level, below and above it were stained by the myelin sheath and cresyl violet methods. Frozen transverse and longitudinal sections from the same areas were stained by the myelin sheath, Holzer, Sudan III and Bielschowsky methods.

Microscopic Examination.—In the myelin sheath preparation, the sections of the spinal cord between the fifth and sixth dorsal segments showed thickening of the meninges and extensive demyelination of all the fiber tracts (Fig. 1, *D*) with slight sparing of a few of the white fibers in the gray matter (Fig. 1, *D*). In sections at the fourth dorsal segment all the fiber tracts, except for the fibers of the gray matter and for a few fibers bordering the posterior and anterior horns, were completely demyelinated (Fig. 1, *C*). At the first and second thoracic segments there was demyelination of the fasciculi gracilis and cuneatus, the former more than the latter, and of the direct and indirect cerebellar and part of the spinothalamic tracts (Fig. 1, *B*). Sections above this level merely showed an ascending degeneration of the fasciculus gracilis and the spinocerebellar tracts (Fig. 1, *A*). In sections immediately below the complete area of demyelination, there were patchy areas of demyelination of the posterior columns (Fig. 1, *E*) and marked destruction of practically all of the ventrolateral tracts. These had a honeycombed appearance. The ganglion cells showed no pathologic changes. In the Holzer preparation, the fasciculus gracilis on the right side showed an intense area of gliosis (Fig. 2). Slight

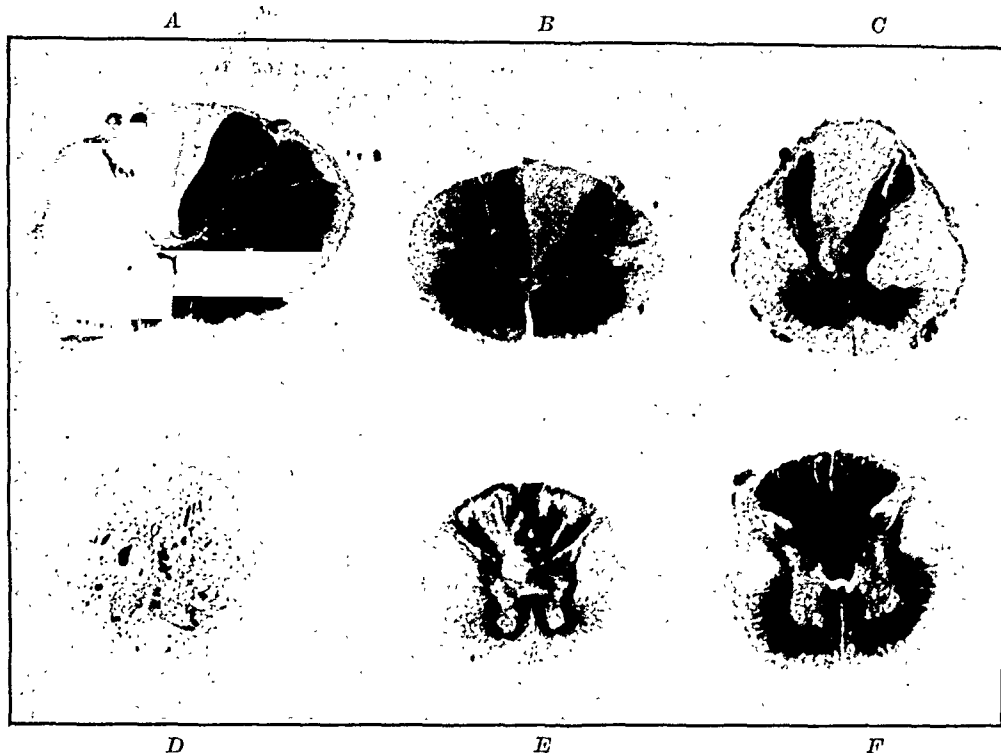


Fig. 1.—Transverse sections of the spinal cord showing complete demyelination of all the fiber tracts from the fourth to the sixth dorsal segment (*C* and *D*). At *D-4* segment (*C*) the fibers of the gray matter and those bordering it appeared spared. The sections above this level showed an ascending degeneration (*A* and *B*). In sections immediately below the complete areas of demyelination, there were patchy areas of degeneration of the posterior columns (*E*) and marked destruction of practically all the ventrolateral tracts. In the lumbosacral region there was a descending degeneration (*F*).

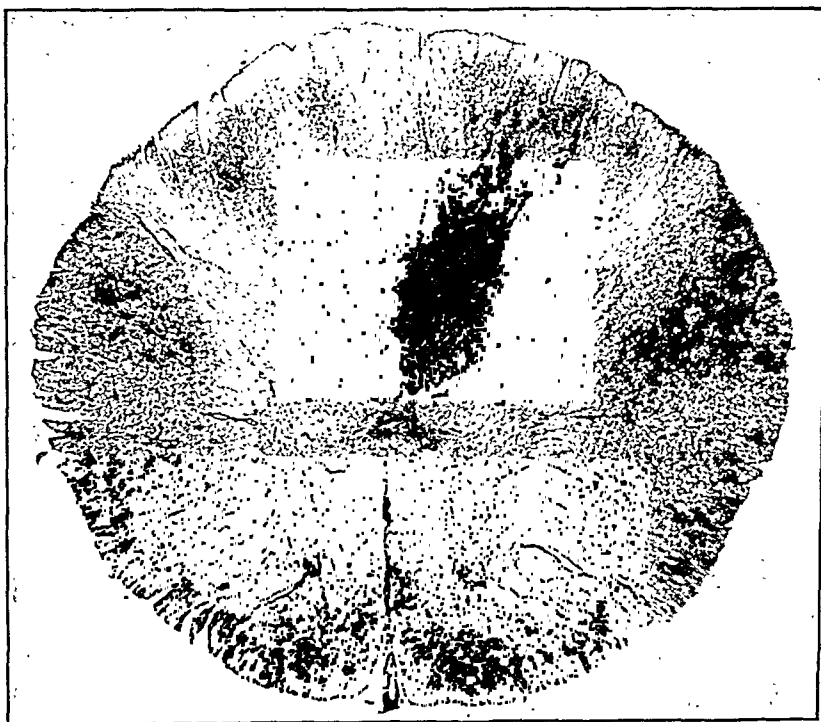


Fig. 2.—Gliosis in area of demyelination. Holzer stain.

gliosis was also found in the lateral and anterior pyramidal tracts. In the lumbosacral region there was a descending demyelination of the lateral pyramidal tracts (Fig. 1, *F*); the anterior pyramidal tracts were only slightly involved (Fig. 1, *F*). With higher magnification the sections at the level of the lesion disclosed a few myelinated fibers within the anterior horns; the other fibers were completely de-



Fig. 3.—Dilatation of vessels lined by a single layer of endothelial cells in area of degeneration. Notice the deposits of iron pigment. Cresyl violet stain. $\times 50$.

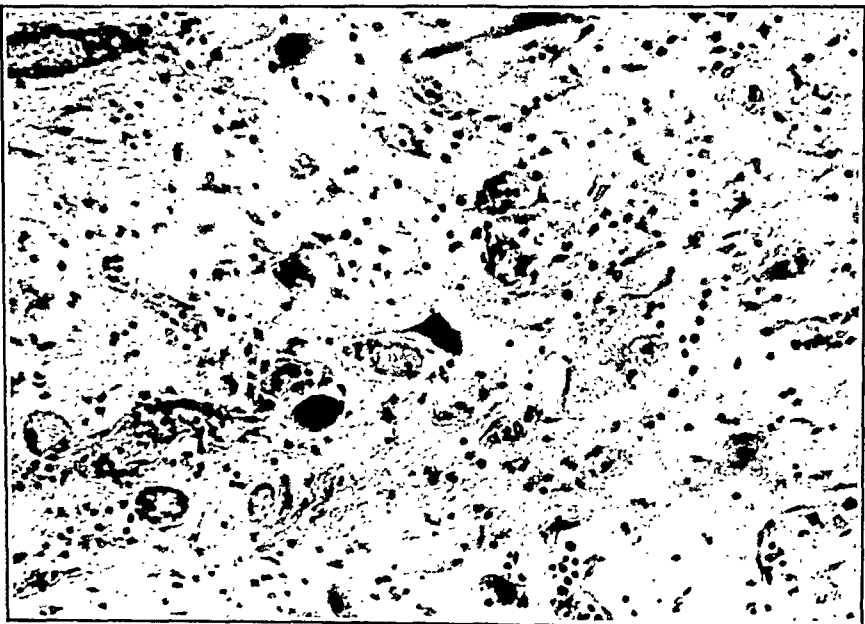


Fig. 4.—Diminution in the number of anterior horn cells. Some appear as shadow cells; others are pyknotic or are completely destroyed. Cresyl violet stain. $\times 200$.

myelinated. The cord at this level did not have a honeycombed appearance but was filled with proliferating and dilated vascular channels (Fig. 3). The gray matter was filled with blood pigment (Fig. 3). Some of the fibers within the anterior roots were slightly demyelinated. In the cresyl violet preparation, the meninges appeared thickened and were filled with polymorphonuclear leucocytes, plasma and

endothelial cells and proliferating arachnoidal and fibroblastic cells. The inflammatory process, although predominantly limited to the meninges, involved slightly the periphery of the cord and the anterior and posterior roots. Proliferation of the smaller intraspinal arteries in the gray and in the white matter was also noted. The entire transverse section of the cord was filled with plump astrocytes, gemästete

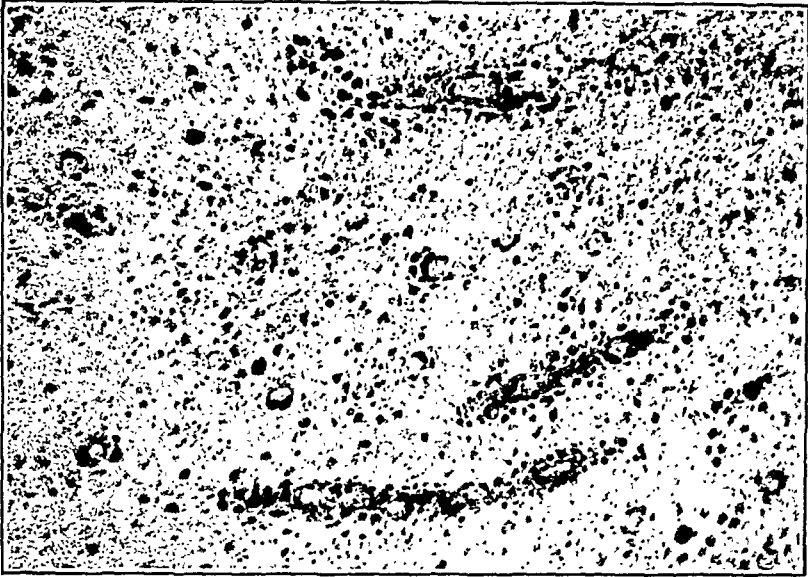


Fig. 5.—Fatty deposits in the cord and in the perivascular spaces. Sudan III stain. $\times 50$.

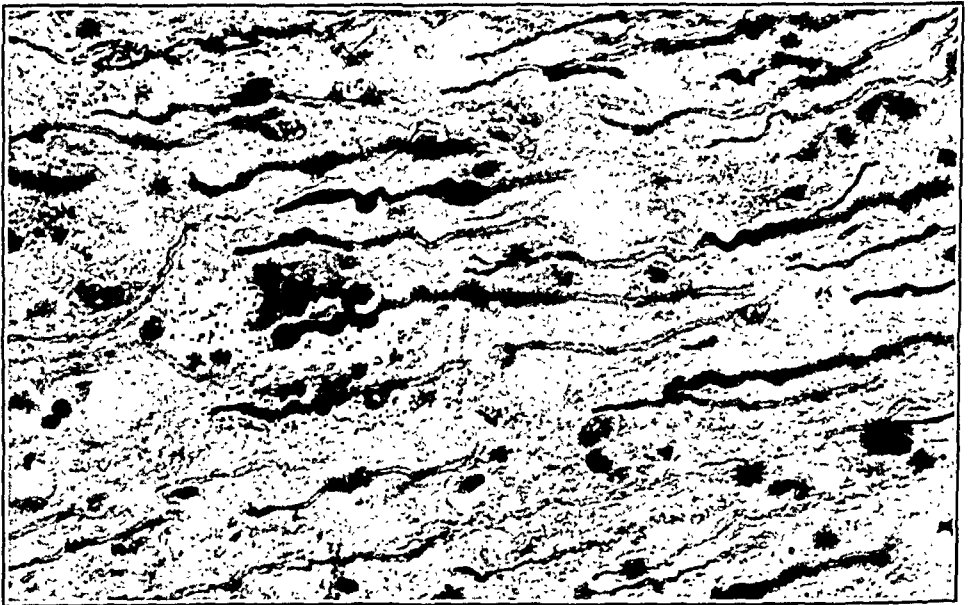


Fig. 6.—Swelling, cork-screw appearance, knoblike projections, beading and destruction of axis cylinders. Longitudinal section. Bielschowsky stain. $\times 400$.

glia cells and occasionally compound granular corpuscles. The ganglion cells of the gray matter were diminished in number and showed various pathologic changes such as shadow cells, complete chromatolysis, shrinkage and pyknosis (Fig. 4). Some of the anterior horn cells were well preserved. In the sections stained with the Sudan III preparation, the areas of demyelination were filled with compound granular corpuscles, loaded with fat. Some of these showed a tendency to collect in the

perivascular spaces (Fig. 5). The gray matter at this level contained small fatty deposits. In the longitudinal sections, the myelin sheaths showed various types of pathologic changes, such as swelling, fragmentation or complete disintegration, while in the Bielschowsky preparation the axis cylinders were either swollen, beaded, tortuous, or fragmented (Fig. 6). Knob-like projections and corkscrew processes were also noted. At the fourth dorsal segment the pathologic process, except for the sparing of the white fibers in the gray matter, was the same. At this level, however, in the cresyl violet preparation, there were no dilated vascular channels and no extravasation of blood or collections of blood pigment. The ganglion cells, although some showed pathologic changes, were in general better preserved. The cord was filled with numerous glia cells of the astrocytic variety; compound granular corpuscles and plump astrocytes were more prominent at the periphery of the cord. In the cresyl violet preparation of the upper thoracic and lower cervical regions, as at the fifth and sixth dorsal segments, there were dilated vascular channels, accumulation of blood pigment, and moderate pathologic changes in the ganglion cells.

COMMENT

The history of an antecedent osteomyelitis and the onset with pain in the back and girdle sensations suggested to some observers an extramedullary process, possibly a recurrence of the osteomyelitis in one of the vertebrae. The roentgen studies, the cerebrospinal fluid findings, and the negative results of laminectomy ruled out this diagnosis. The condition was later considered to be either a vascular myelopathy or a myelopathy due to pregnancy. Clinically, the patient presented a level lesion of the spinal cord, unless one is willing to accept as evidence of dissemination the ocular movements, described at one time as nystagmoid, and later as true nystagmus. In view of the trophic ulcer and the cystitis, it was impossible to determine on clinical grounds whether the progression in the neurologic signs was due to an ascending infection, or to the continued activity of the original noxious agent.

The meningo-myelitic process which developed shortly before death must be considered apart from the main pathologic process which was found at the fifth and sixth dorsal segments. The meningitis was the end-result of the ascending infection from the decubitus ulcer and the fistula which extended into the subarachnoid space. The process at the level lesion was myelopathic in nature and consisted of breaking-down of the myelin sheaths and axis cylinders and a moderate gliosis. The numerous proliferating and dilated vascular channels found at this level and in the upper dorsal and lower cervical regions were the end-result of the destruction of the cord and the attempt at repair. Such a process is not uncommonly seen in myelopathies due to toxic processes or vascular disease. The pathologic picture considered in its entirety conformed to that seen in the toxic myelopathies.

CASE 2.—K. N., a primipara, aged twenty-two, was well up to the seventh month of pregnancy in March, 1933. She had been observed every two weeks before that time in a prenatal clinic and found normal in all respects. One morning she felt a sudden pain between the shoulder blades followed soon after by a burning sensa-

tion over the back. A few minutes later she was unable to stand and the lower half of her body felt numb. Sixteen days later a low forceps delivery was carried out. The puerperium was normal. At the maternity hospital, a neurologic examination is said to have disclosed a complete transverse lesion of the cord.

About a month later, she was observed at a neurologic hospital. She then showed a sensory level at the fifth dorsal segment, a paraplegia, bilateral Babinski signs, absent abdominal reflexes, and urinary incontinence. A spinal tap yielded a normal manometric response. The cerebrospinal fluid was normal. A blood count showed a hemoglobin of 58 per cent with 2,860,000 red blood cells. The color index was 1. The smear showed macrocytosis, microcytosis, and poikilocytosis. The bleeding and coagulation time was normal. The test for fragility of the red blood cells was interpreted as showing markedly increased fragility (onset at 0.48 per cent, complete at 0.38 per cent). The gastric analysis showed absence of free hydrochloric acid.

The patient was given iron compounds and responded very well. Her course was complicated by the development of a cystitis, following upon the initial retention of urine and subsequent overflow incontinence. Gradually she improved.

The impression at the time was that the patient had suffered either from an atypical hematomyelia or from thrombosis of the anterior spinal artery.

She was admitted to the Montefiore Hospital in November, 1933. At that time she showed a sensory level at the fourth dorsal dermatome, with diminution of all forms of sensation below that point. The motor status showed a spastic paraparesis in extension with occasional spontaneous flexion movements in the limbs. The deep reflexes were absent and the Babinski sign was bilaterally present. There was persistence of urinary incontinence and of cystitis. The gastric analysis again showed an achlorhydria. The red blood count was now 4,250,000 and the hemoglobin 75 per cent.

The patient was observed for six months at the hospital. She showed signs of improvement during that period. Her status shortly before her discharge disclosed the following findings: The patient was able to stand unsupported and walked with the aid of a cane. There were occasional urgency of urination and incontinence. The motor status was unchanged. Sensation: There was a sensory level for pain and temperature at the fourth dorsal dermatome, the disturbances being less marked than they were. Touch was normally perceived. Vibration was very slightly diminished below the level. Position sense was intact except for occasional errors in the toes of the left foot.

COMMENT

In this case there was, in addition to the neurologic disorder, an abnormal hematologic picture. The absence of free hydrochloric acid and the favorable response to therapy with iron suggested a hypochromic anemia, such as not infrequently sets in during pregnancy. The high color index was not characteristic of this condition, however. It was the opinion of the hematologist that a secondary anemia of pregnancy existed. Whether the same factor which precipitated the myelopathy also was responsible for the abnormal blood picture remains an open question.

In the absence of histologic studies, one can merely speculate on the character of the underlying pathology in this case. A vascular lesion, perhaps a thrombosis of a spinal vessel, was considered by some ob-

servers. That a thrombosis of a spinal vessel produced this picture appears to us extremely unlikely, since the area affected does not correspond to the distribution of any one spinal vessel. A hemorrhage into the substance of the cord is a possibility. As will be pointed out below, however, the occurrence of a hemorrhage into the cord would not necessarily rule out a toxic factor as the primary cause of the disturbance.

DISCUSSION

From the clinical standpoint, the subject of myelopathy of pregnancy was dealt with comprehensively by Hösslin¹ in 1904. He pointed out the necessity of distinguishing a true myelopathy of pregnancy, in which there is a direct causal relationship between the pregnancy and the myelopathy, from other conditions in which the pregnancy is merely coincidental, as in tumors of the spinal cord, or disorders in which the pregnancy acts merely to precipitate or to exacerbate an independent neurologic disease, such as multiple sclerosis. Hösslin cited twenty cases of myelopathy of pregnancy, in five of which the condition recurred in subsequent pregnancies. In one instance, the patient, after three normal pregnancies, suffered five attacks of myelopathy, three of them occurring during pregnancy and two unassociated with gestation. In another case, myelopathy occurred soon after the termination of the sixth pregnancy, in the third month of the seventh pregnancy, and again shortly after the eighth delivery. Similarly, in the case of Windscheid, myelopathy set in after the first delivery, with a recurrence four weeks following the second delivery. Hösslin thought that there was sufficient evidence to indicate an immediate causal relationship between the pregnancy and the myelopathy, and postulated toxins liberated during pregnancy or the puerperium as the responsible agent.

Since Hösslin's contribution, several reports on this subject have appeared sporadically: Rosenberger and Schmincke,² Krupp,³ Schumann and Fist,⁴ Good,⁵ Marinesco,⁶ Alpers and Palmers,⁷ Spitzer,⁸ Frayman,⁹ and Hassin and Ettleson.¹⁰ Spitzer, reviewing the subject in 1932, was able to collect only twenty additional cases since Hösslin's report of twenty cases in 1904.

Clinically, myelopathy of pregnancy is characterized by the following features: The condition may develop in the course of the first pregnancy or only after several normal pregnancies have already occurred; the onset may occur during pregnancy, immediately postpartum, or later in the puerperium. While it may set in during any part of pregnancy, it more commonly occurs during the latter half. The onset may be sudden or gradual. Hösslin expressed the opinion that the more acute the onset, the worse the prognosis, but that this is not invariably so is evident from a study of our own cases in which the more severe and eventually fatal myelopathy followed upon a gradual onset. Usually

there is no rise in temperature, nor are there any other constitutional signs to suggest an infectious process. The neurologic picture varies. There may be signs of a level lesion of the spinal cord, complete or incomplete, or the process may involve the cord diffusely at different levels. Spitzer distinguishes a cervical, dorsal, lumbosacral and disseminated type of myelopathy as well as a funicular type in which the dorsal and lateral columns are involved. In some cases the medulla oblongata has been implicated. The outcome also varies. There may be complete restitution of function, partial recovery, or progression and death, the latter resulting usually from complicating bed sores or cystitis with ascending infection. In Spitzer's review of forty cases, the mortality was 22.5 per cent. The tendency to recidivism in subsequent pregnancies has already been mentioned. In this respect, myelopathy of pregnancy resembles certain other complications of pregnancy, such as peripheral neuritis, lesions of the optic nerve, and icterus neonatorum.

Considerable diversity of opinion exists regarding the underlying etiologic factors in myelopathy of pregnancy. A toxic or an infectious process has been held responsible by some observers. Others favor a vascular etiology without specifying further just what the basis of this vascular disturbance may be.

It seems to us difficult to explain the occurrence of myelopathy of pregnancy on the basis of an infectious process; not because of the customary absence of any history or signs pointing to an infectious disease—since it is well recognized that infections of the nervous system may occur without frank evidence of infection elsewhere in the body—but because of the tendency of a considerable proportion of these cases to recur in subsequent pregnancies. The dramatic improvement that takes place in many of the cases after the pregnancy is interrupted or labor occurs also suggests an intimate relationship between pregnancy and a moderate myelopathy, rather than some fortuitous infectious process. As already indicated by one of us (Davison¹⁴), mild toxic substances may not produce extensive and permanent damage to the spinal cord.

It is conceivable that the termination of pregnancy suspends the further action of the toxin before irreparable changes have occurred, thus permitting reparative processes to take place. The same objections apply to a vascular etiology. One is led to inquire what kind of vascular disease would make its appearance during a pregnancy, clear up sufficiently following this to allow partial or complete restitution of function, only to reappear in a succeeding pregnancy. In those cases in which a complete or almost complete level lesion exists, it is difficult to understand how occlusion of one spinal vessel can be held responsible, since the cord is supplied by the anterior and posterior spinal arteries as well as by arteries entering at the lateral margins.

To assume that all of the vessels at one level of the cord are simultaneously involved, while vessels at other levels are spared, seems strained.

Accepting, for the moment, the possibility of a vascular etiology, one is also led to inquire whether the vascular disease itself must not be secondary to some other factor since, in these cases, there is no preexisting generalized vascular disease, hypertension, syphilis, cardiac pathology, or any other condition predisposing to a vascular accident.

One argument adduced for the likelihood of vascular disease of the cord is the sharp level lesion that occurs in some of these cases. It is generally held that toxic and infectious processes give rise to more or less disseminated lesions of the cord, and that a sharp level lesion indicates implication of a vessel at that level. The occurrence of a level lesion would not rule out a toxic process, however, if the vascular pathology were secondary to the action of toxins on the vessel wall. In that case, instead of thinking in terms of a vascular *or* a toxic factor, one must think in terms of a vascular *and* a toxic factor.

At the risk of venturing further into fields of speculation, still another possibility that must be entertained as at least a contributory factor in myelopathy of pregnancy is some form of dietary insufficiency. Numerous studies recently made point to a vitamin B deficiency as the underlying factor in gestational neuritis. In these cases hyperemesis is almost constantly present, so that a vitamin deficiency undoubtedly exists. While vomiting is not a factor in the cases of myelopathy of pregnancy, the possibility of a dietary inadequacy is not thereby precluded. During pregnancy the vitamin requirements of the mother are increased. At the same time there may be faulty metabolism and absorption of foods due to the diminished secretion of gastric juices. In experimental avitaminosis, finally, lesions of the nervous system, both degenerative and hemorrhagic, and hence similar to those found in myelopathy of pregnancy, have been observed.

It would seem reasonable to suppose that pathologic studies might shed some light on this obscure problem. That the problem from the standpoint of the pathologist also offers difficulties is soon apparent, since various pathologists, confronted by certain findings in the spinal cord, may offer entirely different interpretations of these findings. It is known, for example, that in toxic myelopathy of infectious myelitis, circulatory disturbances may play a rôle and produce a picture indistinguishable from ordinary vascular myelopathy. In cases in which some pathologists would hold the vascular supply primarily responsible, others might question whether the blood vessels have not been concomitantly affected with the parenchyma, or even secondarily affected after the parenchyma was already damaged. The fact that

the pathologist views the specimen long after the acute process has subsided does not simplify matters. The question also whether a process is infectious or not is often open to dispute. In the chronic phase, perivascular infiltration may have disappeared, while on the other hand, the mere presence of such an infiltration need not indicate a true infectious process but merely a response to tissue damage of any sort, the so-called "symptomatic inflammation" of Spielmeyer. In this connection, one of us (Davison¹⁵) has pointed out the need for caution in interpreting perivascular infiltrations as evidence of an inflammatory process, since special histologic studies have shown that cells considered as lymphocytes may really be fat-laden glia cells (compound granular corpuscles).

Bearing all these difficulties in mind, we have ventured an interpretation of the histopathologic findings in our case and concluded that the process is toxic in nature. At the same time we envisage the possibility that some form of vitamin deficiency may be at least a contributory factor.

The number of cases of myelopathy of pregnancy that have been studied with sufficient care to serve as a basis of comparison with our case is exceedingly small. For this reason it is advisable to review them briefly.

In the case described by Hamill,¹² the disease occurred in a primipara fourteen days after labor. The lower limbs were first involved, later the upper limbs. There was a sensory level slightly above the umbilical region, with anesthesia below that point. The patient died five days after the onset, in coma. Postmortem examination disclosed an acute diffuse hemorrhagic "myelitis," the lower dorsal and upper lumbar regions of the cord being most affected. In these regions the nerve fibers had disappeared; the cells in the anterior horns of the gray matter were swollen and shapeless. Rosenberger and Schmincke² described a case of "myelitis" occurring in a primipara during the third month of pregnancy. At first there was involvement of the lower limbs; this later spread to the upper limbs. There were a sensory level at the region of the nipples, bilateral pyramidal tract signs, and vesical disturbances. Later, bulbar signs appeared. The histologic study of the spinal cord disclosed disseminated lesions of a "parenchymatous degenerative" nature, more marked in the cervical and less marked in the thoracic and lumbar segments. Both the gray and the white matter were affected. Bauch¹³ described the case of a primipara who, eight days after labor, developed bulbar signs in the form of dysarthria and dysphagia followed shortly by diplopia. Death occurred within a few days. Histologic study disclosed perivascular infiltrations of lymphocytes in the medulla oblongata and in the quadrigeminal plate. In the upper cervical region of the spinal cord, similar perivascular cuffing was present in the gray and white substance and in the meninges. The ganglion cells were unevenly colored, but did not show frank signs of degeneration. Hassin and Ettleson¹⁰ more recently reported a case of myelopathy occurring during pregnancy in a girl of nineteen. A history of antecedent syphilis and the occurrence of an upper respiratory infection at the time of onset of the myelopathy were complicating factors. The neurologic status showed a level lesion with a flaccid paraplegia; pain and temperature sensations were lost up to the level of the umbilicus; there was also vesical incontinence. Infection from bed sores led to death. There was no glossitis nor a blood picture

characteristic of pernicious anemia. A gastric analysis was not performed. Histologic study showed changes in the lateral columns with only mild involvement of the posterior columns of the cord. "The changes were not those of syphilis or of inflammation. . . They were degenerative, of the type observed in subacute combined degeneration of the spinal cord; they resembled nothing else." The authors thought the picture of subacute combined degeneration of the cord found in this case might be a manifestation of a toxemia of pregnancy. Of these cases, the one reported by Bauch clinically and pathologically suggests the diagnosis of a bulbar poliomyelitis. In the three remaining cases the pathologic process was degenerative or hemorrhagic in nature. These resembled in many respects our first case. The etiology was most likely toxic in nature.

SUMMARY AND CONCLUSIONS

One case of myelopathy of pregnancy, studied clinicopathologically, and another observed clinically, are reported.

A survey of previous histologic reports has shown that the underlying pathologic process is degenerative or hemorrhagic in nature.

Reasons for believing that myelopathy of pregnancy may be due to some toxic factor, the exact nature of which remains as yet undetermined, and that vitamin deficiency may play a contributory rôle in the production of the disease, have been presented.

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Burr, Hill and Allen as the first demonstrated by means of a vacuum-tube potentiometer, in the rabbit, a change in the electrical potential immediately preceding the rupture of a ripe follicle. Reboul, Friedgood, and Davis confirmed these significant observations on rabbits.

Rock, Reboul, and Wiggers describe in this paper in great detail a parallel observation made on a regularly menstruating woman. Histologic examination of follicular tissue and endometrium obtained during a required laparotomy proved that voltage changes, quite similar to those observed in the ovulating rabbit, also in this patient seemed dependent upon the rupture of a mature follicle.

HUGO EHRENFEST.

FUNCTIONAL UTERINE BLEEDING WITH SPECIAL REFERENCE TO THAT ASSOCIATED WITH SECRETORY ENDOMETRIUM

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FROM time to time there has appeared in the literature evidence which would seek to explain functional uterine bleeding on a basis other than that of endometrial hyperplasia. Whether or not such an entity or entities exist is a matter of controversy. Graves¹ states that "typical dysfunctional metrorrhagia is almost always associated with endometrial hyperplasia." Novak² agrees and says that "histologic examination of the endometrium in cases of functional hemorrhage, almost always reveals the picture designated as hyperplasia of the endometrium."

On the other hand there have been a series of papers tending to show that functional uterine bleeding can occur in the absence of an endometrial picture of hyperplasia. However, there is a conspicuous absence of agreement among these authors as to the nature of the abnormalities (Table I).

TABLE I. THE INCIDENCE OF FUNCTIONAL UTERINE BLEEDING ASSOCIATED WITH HYPERPLASTIC AND NONHYPERPLASTIC ENDOMETRIUM

	NO. CASES	HYPERPLASIA		NONHYPERPLASIA	
Kaufmann and Hoeck, 1926 ³	133	45	43%	75	55%
Fluhmann, 1929 ⁴	90	49	54%	41	46%
Anspach and Hoffman, 1934 ⁵	97	53	55%	44	45%
Keene and Payne, 1934 ⁶	500		23%		77%
Traut and Kuder, 1935 ⁷	100	68	68%	32	32%
Hamblen, 1936 ⁸	358	102	28%	256	72%
Present study, 1937	83	52	63%	31	37%

The great variation in the incidence of hyperplasia probably depends on individual opinion in diagnosis of hyperplastic endometrium and the variation in types of cases included in the nonhyperplastic group.

Pankow⁹ in 1924 described 3 cases of abnormal bleeding in which he thought there was a characteristic endometrial picture. Here the endometrium had no epithelial surface. The stroma was compact and infiltrated with round cells and blood. The glands were collapsed, but there was no evidence of secretion. Pankow supposed that there was a delay in the regeneration of the endometrium.

In the study of Kaufmann and Hoeck, published in 1926, the pathologic findings of the endometrium in 133 cases with abnormally profuse bleeding are described in detail. They point out that there is no characteristic clinical history associated with any of the pathologic pictures presented. Hyperplasia was found in 58 cases. The remainder are grouped into 6 types as follows:

1. Six cases showed abnormal shedding of the endometrium. The surface is irregular and humpy. The stromal cells are compact and the nuclei are small. The

glands assume bizarre forms and are many times star-shaped. The lumina are filled with secretion. The protoplasmic edge of the epithelium is irregular, the nuclei are at the base of the cell and glycogen can be stained in the secretion and in the cells. The authors consider that there is an incongruity between the actively functioning glands and the inactive appearing stroma.

2. In 14 cases the diagnosis of "functionless endometrium" is made. Here the endometrium is covered with a smooth surface. The glands are procumbent, but without irregularity in form. The epithelium is cylindrical, the protoplasmic edge is sharp and the protoplasm itself is dark and not translucent. The nuclei occupy the greater part of the cell. The stroma is rich in nuclei and fibers. The capillaries are abnormally dilated. On the one hand this is differentiated from interval endometrium by the delicately active stroma and clear cytoplasm of the latter. On the other hand it is differentiated from atrophic endometrium by the general shrinking of the stroma of the latter and the atrophic appearing nuclei. In this group of cases, the correlation between the ovarian cycle and that of the uterus seems to be lost and there is no evidence of any cyclic activity on the part of the endometrium.

3. In 20 cases, most of them at the menopause, a diagnosis of atrophic endometrium is made. Here there is a generalized shrinking process of the stroma with collagen fibers and shrunken nuclei. The glands are scattered irregularly through the rigid stroma.

4. In 13 cases the endometrium is described as normal except for congestion. However, in only two cases could a cause for the congestion be discovered. In these the patients were suffering from myocardial insufficiency. A restoration of circulatory compensation corrected the irregular bleeding.

5. In 18 cases the endometrium is considered normal. The phase is not described.

6. In 4 there was a marked chronic endometritis.

It will be noted that Kaufmann and Hoeck have drawn fine pathologic lines. In the present study this classification was kept in mind, but it must be said that it was difficult to identify these finely differentiated endometrial types.

Baniecki,¹⁰ from the same Berlin clinic as the above authors, published a series of cases (32) with the characteristic endometrial findings of irregular shedding as originally described by Kaufmann and Hoeck. The clinical histories and the microscopic findings with several photomicrographs are presented.

In this country Fluhmann found that there was little correlation between any one type of bleeding history and a special type of endometrium. In 90 cases Fluhmann found 6 endometrial pictures: hyperplasia, 54 per cent; endometrial polyp, 3 per cent; simple hypertrophy of the endometrium, 2 per cent; endometritis, 8 per cent; atrophy, 6 per cent; normal endometrium, 27 per cent. In this latter group no statement is made of the endometrial phase. In contradistinction to Kaufmann and Hoeck and to Baniecki, Fluhmann did not diagnose irregular shedding, functionless endometrium or edematous endometrium although there is no reference to either of these papers in Fluhmann's article. In over 85 per cent of his cases of functional bleeding, the endometrium was found to be either hyperplastic or normal. As noted above, Fluhmann included endometrial polyps and endometritis in his series of functional bleeding. Many authors would exclude these from such a group and if this were done, in over 91 per cent of his cases the endometrium would be either normal or hyperplastic.

Anspach and Hoffman in 1934 described the endometrial findings in 97 cases of functional bleeding. In agreement with practically everyone who has published on this subject, they found that there was no correlation between any one type of bleeding and the endometrial picture; 31 are associated with premenstrual endometrium. This high percentage (70 per cent) may be due to the fact that care

was taken to curette before the expected period of bleeding. Where bleeding was irregular, curettage was performed irrespective of the flow. The remaining cases showed either normal interval or atrophic endometrium. These workers noted some variation in the phase of the endometrium in different portions of the scrapings, but did not consider them significant enough to group together as an entity.

Keene and Payne also in 1934 reported the findings in 500 cases of functional uterine bleeding. All types of bleeding history are represented. Table II from their paper summarizes their results. There was a 23 per cent incidence of hyperplasia in the whole series. Phases of the normal endometrium are not reported.

TABLE II

	NO. CASES	NORMAL ENDOME- TRIUM	HYPER- PLASIA	INSUFF. TISSUE	EDEMATOUS ENDOME- TRIUM	CHRONIC ENDOME- TRITIS
		%	%	%	%	%
Menorrhagia group	190	76	12	10	1.5	0.5
Metrorrhagia group	310	56	30	10	1.5	2.5

Traut and Kuder in 1935 described 11 patients, the endometrial findings in whom corresponded with that described by Kaufmann and Hoeck and enlarged upon by Baniecki and called by them irregular shedding of the endometrium. Traut and Kuder state, "it would seem probable that in this type of menorrhagia we may be dealing with nothing more complicated than a very much prolonged menstrual period." With this we fully agree and would further point out that the description given by them and by the earlier workers could apply to endometrium obtained from a normally menstruating uterus. In our opinion there is nothing characteristic about this endometrium which would allow it to be set apart as a pathologic entity.

In this same paper Traut and Kuder describe a series of 21 cases of a new pathologic group and called by them irregular ripening of the endometrium. The pathologic point of departure is a variability of the phases of the endometrium in different areas of the same uterus. In order to make this diagnosis, both a secretory and nonsecretory phase must be identified. While the present study is primarily concerned with functional uterine bleeding from secretory endometrium, we have encountered only minor degrees of variability. Many further observations must decide the significance of this possibility. In several cases we have studied, in which the diagnosis of irregular ripening of the endometrium was considered, we could not convince ourselves that relatively large bits of tissue showing interval or mild hyperplasia in otherwise secretory endometrium were not fragments of endometrial polyps. The diagnosis of endometrial polyp from curettings is not made as frequently as one might suppose, considering the not infrequent finding of polyps in uteruses where the whole specimen is available for study.

Hamblen has recently attempted a functional classification of uterine bleeding from a histologic examination of the endometrium in correlation with clinical data and therapeutic response. His classification is based on the theory that menstrual bleeding occurs during cyclic phases of relative estrin deficiency. He likewise assumes that irregular and often acyclic phases of relative estrin deficiency occur resulting in functional irregularities.

Table III, compiled from Hamblen, summarizes the results in 358 patients divided according to whether or not the patient was bleeding when the specimen was obtained.

A given case is diagnosed as belonging to any of these functional classes according to its endometrial pattern. Anestrin phase is diagnosed from atrophic endometrium, regular estrin phase from post-menstrual or interval endometrium. An irregular pattern with individ-

TABLE III

	BLEEDING	NOT BLEEDING
Hypoestrin or anestrin phase	38	38
Regular estrin phase	6	10
Phase of irregular estrin action	34	60
Phase of prolonged acyclic estrin action	68	34
Progestational phase following irregular estrin action	5	35
Progestational phase following prolonged acyclic estrin action	4	9
Progestational bleeding phase with irregular or incomplete tissue shedding	8	—
Progestational bleeding phase with usual tissue loss	9	—

ual variations in different portions of the endometrium is thought to result from "irregular" estrin action. Prolonged estrin action yields classical endometrial hyperplasia. Patchy progestational change in either of the latter two types places that case in the appropriate group. The two progestational bleeding phases depend upon whether or not there is abnormal tissue loss.

A functional classification of uterine bleeding is very desirable, and useful as a working guide to therapy. However, before such a classification is finally worked out, many more endocrinologic observations must be made. The assumption of what is happening to the hormones by an examination of the endometrium may be misleading.

FUNCTIONAL BLEEDING WITH SECRETORY ENDOMETRIUM

A consideration of the literature serves to show the variation in the endometrial findings especially those cases not associated with hyperplasia. As pointed out some authors deny the existence of functional bleeding except in the presence of endometrial hyperplasia. Therefore as distinct from hyperplasia we have studied a series of 41 cases from the records of the Gynecological Department of the Johns Hopkins Hospital in which functional uterine bleeding seems to be associated with secretory endometrium. As far as can be determined by bimanual and speculum examination all local causes such as cervical polyps, myomas, carcinoma, inflammatory conditions of the uterus and adnexa were excluded. Two cases in which small cystic ovaries were palpated and which were available for examination are included. Cases with hypertension were not included.

INCIDENCE

From histologic examination of the endometrium, we have found it impossible to group all cases into those associated with hyperplasia or those associated with secretory endometrium. There is a group remain-

ing diagnosed as postmenstrual, interval or atrophic. It is not felt that this residue should be subdivided as entities for it is clear that some cases in this group may in reality belong to either of the other two. Postmenstrual or interval endometrium may be found in a given case which at a previous curetting had shown classical endometrial hyperplasia. This does not necessarily mean that there has been a change in the endocrinologic background. This finding would be possible if the characteristic hyperplasia pattern had been shed and there had not yet been time to rebuild beyond the normal appearing postmenstrual or interval pattern. On the other hand it is quite possible that these same cases might, had they been curetted at another time, show secretory change. Atrophic endometrium is normal after the menopause. Many authors have made this diagnosis in abnormally bleeding women during active menstrual life. When atrophic appearing endometrium is found under these conditions it may represent scanty material obtained from the basalis and perhaps a little from the functionalis and thus the tell tale part of the endometrium has already bled away, so that here too these cases may in reality belong to either the hyperplasia or secretory group.

With these facts in mind a consecutive series of 83 cases of functional bleeding was studied, in order to determine the incidence in this clinic. This series of 83 cases is separate and distinct from the 41 cases chiefly studied in this report. The following diagnoses were made:

1. Endometrial hyperplasia	52	63%
2. Secretory endometrium (late interval, premenstrual, menstruating)	14	17%
3. Belonging to neither (1) or (2) (postmenstrual, interval, atrophic)	17	20%

AGE OF OCCURRENCE

Functional uterine bleeding with secretory endometrium may occur almost at any time from the menarche to the menopause. The extremes in the series under analysis are seventeen and forty-nine. It should be pointed out that these figures apply to the ages of the patients when they were seen at the hospital and not to the age when abnormal bleeding began. This latter age can easily be determined from a study of the clinical history. It is obvious that these two figures in any one case may differ by several years. Table IV shows the number of cases by five-year intervals both on admission to the hospital and at the onset of abnormal bleeding.

This reveals an interesting clinical fact, namely that over half the cases (61 per cent) occur between the ages of twenty-five and thirty-nine, in sharp contrast to the age incidence of hyperplasia bleeding which occurs at the extremes of menstrual life and especially over forty. In Schroeder's series of hyperplasia, 77.8 per cent are over the age of

forty. On the other hand 76.6 per cent of this series are below the age of forty. Taking into consideration the much more frequent actual occurrence of hyperplasia, we see that if a woman under the age of forty is found to have functional uterine bleeding there is almost an even chance that secretory endometrium will be found. However, if she is over the age of forty the chances are overwhelmingly in favor of hyperplasia.

TABLE IV

AGE	NO. CASES UPON HOSPITALIZATION		NO. CASES AT ONSET OF SYMPTOMS	
Below 15	0		3	7%
15-19	2	5%	4	10%
20-24	4	10%	3	7%
25-29	8	18%	7	16%
30-34	7	16%	9	25%
35-39	10	28%	7	16%
40-44	7	16%	6	14%
45-49	3	7%	2	5%
	41		41	

CLINICAL HISTORY

There is no characteristic menstrual history although there are three more or less distinct types of alteration:

1. Increase in amount and duration of flow with normal interval with or without intermenstrual bleeding.
2. Increase in amount and duration of flow with shortened interval with or without intermenstrual bleeding.
3. Irregular bleeding.

1. The simplest alteration is an increase in the length and amount of flow with no alteration in the interval. Twenty patients fall into this group. For this study no patient was included that had bled less than eight days. This excluded a large series of borderline cases where periods were increased from three to four days to from five to seven days and a group in which the patients complained of an increase in flow with a normal duration. It should be pointed out that although the alteration was considered too trivial to be included in the study, it was considered important enough by the patient to consult a physician. Such cases perhaps represent the earliest alteration from normal. Seven patients with simple menorrhagia also complained of intermenstrual bleeding.

2. In 10 patients the interval was shortened, in one patient being fourteen days. In the majority of these menstruation was also prolonged.

3. Eleven patients had irregular bleeding, one as long as forty-two days. In many of these the first alteration was menorrhagia, then shortening of the interval and finally complete derangement of the cycle.

ENDOMETRIAL FINDINGS

Hitschmann and Adler were among the first to correlate the cyclic changes in the endometrium. These authors suggested a division of the menstrual cycle into 4 phases and with modification this division is used here. The interval phase is considered to have two subdivisions. In *early interval*, the surface epithelium is columnar, the glands are still relatively straight and the stroma compact. There is no evidence of a secretion. In *late interval*, the surface epithelium is still columnar and tall. The glands are wider and more tortuous and the epithelium of the glands has begun to show evidence of secretion as droplets in the cytoplasm. No endometrium can properly be considered as late interval unless evidence of secretion is found. Such endometrium would usually be present, from soon after ovulation until the premenstrual change takes place, this happening according to Novak about the beginning of the last week of the cycle.

In the premenstrual phase the surface epithelium is intact in the curettings and retains its high columnar form. The glands are extremely convoluted with a general corkscrew pattern. The lining cells are now quite flat, the inner border is irregular and the cytoplasm seems to melt into the gland lumen. The stroma cells are much larger and may resemble the early decidual cells of pregnancy. This resemblance may be so great that various authors have referred to them as pseudodecidual cells.

In menstruating endometrium the surface epithelium is normally absent. The glands are collapsed. The lining cells are flat and still show by the irregular border and cytoplasmic droplets the evidence of secretion. The stroma is shrunken, the cells are small and there is a general influx of wandering cells.

In the 41 cases of this series, the endometrium obtained from curettings showed late interval in 10 instances, premenstrual in 24, menstrual in 7, while in 6 there were minor variations as will be described. Some cases have more than one curetting. The presence or absence of bleeding as well as the time of curettage in relation to the time of the menstrual cycle is of great importance in interpreting the endometrial findings. In some cases the bleeding is so irregular that the fundamental menstrual rhythm cannot be determined.

In the 10 cases in which a clinical history of shortened menstrual interval was obtained, the diagnosis of late interval endometrium was made in 8 patients and premenstrual in 2. In all of these, in addition to the shortened interval, there was menorrhagia and in 2 instances there was a slight amount of intermenstrual bleeding. When the findings are considered in relation to the histories of the individual patients, it seems that the interval has been shortened by bleeding occurring from endometrium which had not yet had time to undergo change into premenstrual phase. That this probably happens is illustrated by a forty-six-year-old patient who for six months had been having menorrhagia every three weeks. The patient was curetted on the first day of bleeding, and late interval endometrium was obtained.

There are 20 patients with menorrhagia and a normal interval, among whom are 7 associated with intermenstrual bleeding, not severe enough, however, to mask

the fundamental menstrual rhythm. Six were curetted in the intermenstrual interval. In each of these, normal secretory endometrium was obtained, corresponding to the calculated day of the cycle. One of the patients of the latter group, K. M. (K62153), appeared in the gynecologic dispensary June 25, 1936, complaining of very profuse menstrual periods. Since 1930 a curettage had been done 3 times and also a right oophorectomy and suspension with only temporary relief. Report from the hospital where laparotomy was performed stated that the right ovary was "cystic." It is not known if a pathologic examination was made. The flow was now so profuse that the patient, who was a stenographer, could not work and had to remain in bed during the monthly flow. The physician who saw this patient in the dispensary made a tentative diagnosis of endometrial hyperplasia. Suction curettage, on the twenty-fifth day of the cycle, revealed well-developed premenstrual endometrium.

Six patients were curetted while bleeding. One, curetted on the second menstrual day, showed menstruating endometrium. Two others, one on the first and one on the second menstrual day, showed normal premenstrual findings. Of special interest are the three remaining patients, curetted on the ninth, thirteenth, and twentieth days of a prolonged profuse period. In each case secretory endometrium was obtained.

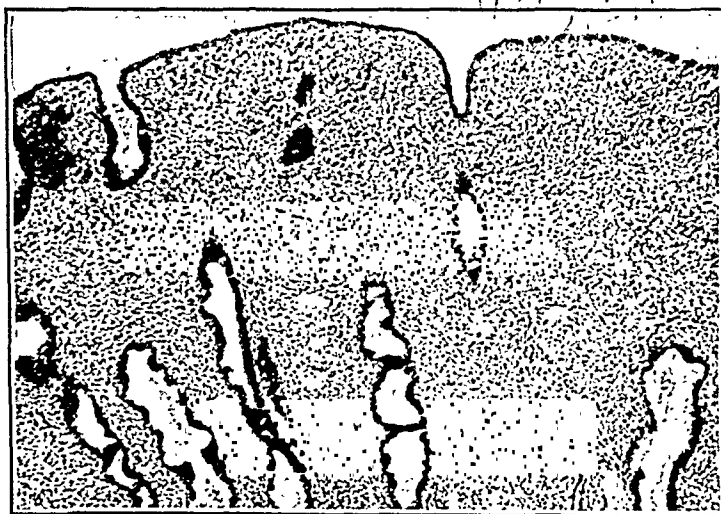


Fig. 14.—(U59694.) Curettings obtained on twenty-first day of continued menstrual period showing interval pattern with secretory epithelium. $\times 75$.

So far it has been assumed that although there has been abnormal bleeding, the endometrium has continued to undergo its usual cycle. However, a consideration of the following case, in which secretory endometrium was obtained on the twentieth day of bleeding suggests an alternate possibility:

A thirty-five-year-old woman (U59694) entered the hospital Dec. 20, 1934, complaining of lower right quadrant pain and menorrhagia. For the past few months periods had been lasting two or three weeks, interrupted occasionally by a period of normal duration. The lower right quadrant pain had been growing steadily worse. Last menstrual period November 30 to present. However, no note is made of bleeding at the ward examination, and it is definitely stated at the time of curettage on December 21 that no bleeding was present, so that the period may have ended. Previous menstrual period October 22 to November 1. Ether examination revealed normal pelvic organs except for a small cystic ovary on the right. As this was not thought to be large enough to cause the patient's lower right quadrant pain, only a curettage was done. The endometrium obtained was markedly secretory, al-

though it was not typical late interval or premenstrual (Fig. 1A). The general pattern was that of interval with slightly tortuous glands, but without the corkscrew premenstrual pattern. The gland cells, however, showed very marked secretory activity. Postoperatively the patient had no further bleeding, but still complained of lower right quadrant pain. Cystoscopy revealed no cause for this in the right kidney or ureter. Accordingly, because of the above-mentioned cystic ovary, laparot-

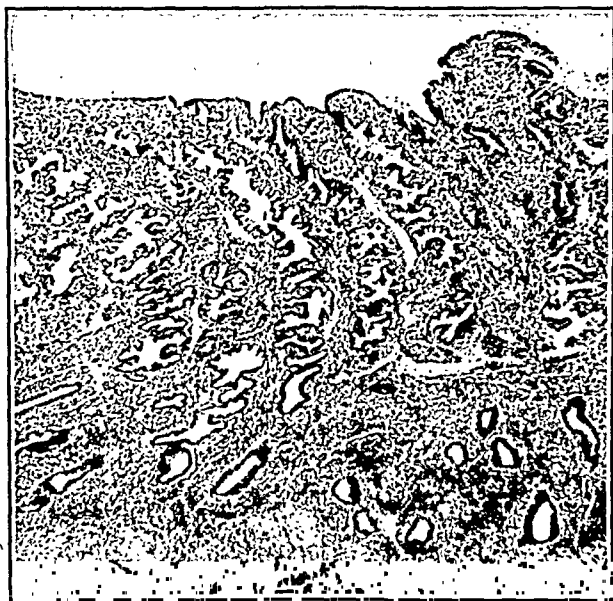


Fig. 1B.—(U59694.) Endometrium twenty-seven days after curettings shown in Fig. 1A. Endometrium only 3 mm. thick and very compact. Cork-screw glands and active secretion. $\times 60$.



Fig. 1C.—(U59694.) Wall of corpus luteum cyst associated with irregular bleeding from secretory endometrium. $\times 75$.

omy was carried out Jan. 17, 1935. The uterus was found to be normal, the left tube and ovary had been removed. There were numerous adhesions binding the right tube and ovary to surrounding structures. There was a right hydrosalpinx about 1 cm. in diameter and in the right ovary was a "small" cyst with a thin yellowish lining. Sections showed normal uterine muscle. The endometrium was not over 3 mm. in depth. The glands had a well-marked corkscrew pattern and

secretory epithelium (Fig. 1B). Section of the right ovary revealed a corpus luteum cyst lined with several layers of lutein cells (Fig. 1C). Diagnosis: Normal uterus, premenstrual endometrium, hydrosalpinx right, corpus luteum cyst of ovary, right. The possible interpretation of this finding will be considered below.

Of the 7 cases of simple menorrhagia associated with intermenstrual bleeding none were curetted while having a menstrual period. Two of these, one on the thirteenth and the other on the twenty-first day showed late interval endometrium. The others, falling between the twenty-second and the twenty-seventh days, showed premenstrual changes.

In one of this latter group there was an associated corpus luteum cyst. The patient (U39499) complained of menorrhagia and slight intermenstrual bleeding of two years' duration. A small mass about 5 cm. in diameter was palpated in the right adnexal region. This was thought to be inflammatory. On the twenty-fourth



Fig. 2A.



Fig. 2B.

Fig. 2A.—(U39499.) Curettings obtained on twenty-fourth day of cycle. Patient complained of menorrhagia of two years' duration. $\times 75$.

Fig. 2B.—(U39499.) Wall of corpus luteum cyst associated with abnormally profuse bleeding from secretory endometrium. Many layers of lutein cells inner border of which is lined by fibroblasts. Coagulated fluid in lumen. $\times 75$.

day of the cycle a curettage and laparotomy were performed. Late interval endometrium was obtained (Fig. 2A). The mass on the right proved to be a cyst in the right ovary measuring 4 cm. in diameter and showing a lining of lutein cells (Fig. 2B).

There were 11 patients bleeding so irregularly that the fundamental menstrual rhythm was obscured. All of these were bleeding when curetted. In 3 instances the diagnosis of menstruating endometrium was made. In the remaining 8 patients although active bleeding had been going on up to thirty-four days, normal premenstrual tissue was obtained. Apparently bleeding was occurring from endometrium which was not being shed as in normal menstruation or at any rate was not being shed to the extent which occurred in normal menstruation.

DISCUSSION

We may summarize the pathologic findings in this series very briefly by stating that functional uterine bleeding may occur from tissue which is indistinguishable from normal secretory endometrium. All secretory phases are represented, late interval, premenstrual and menstrual. An important question immediately arises. Does the presence of secretory endometrium necessarily prove that prolonged estrin action is not an associated condition? This is important because some writers have contended that almost invariably with functional uterine bleeding there is found endometrial hyperplasia thus implying abnormal estrin action. Based on the observations of Schroeder,¹¹ Novak and Martzloff,¹² Burch and others,¹³ it is now generally thought that hyperestrinism and a suppression of ovulation are associated with a pathologic picture of endometrial hyperplasia. Might it not be possible to have functional uterine bleeding associated with hyperestrinism without the suppression of ovulation? A direct attack upon this point would be the determination of blood and urinary estrin in a series of cases of this type. So far as we know this has not been done.

It is likewise impossible to determine this point by an examination of the endometrial tissue. At first thought one might expect the tissue from such a condition to show an excessive proliferative pattern in addition to secretion; in other words the tissue might be expected to have the general pattern of hyperplasia, but exhibiting secretion. However, this is probably not the case, for in early pregnancy where there is a physiologic excess of estrin, the endometrium shows an exaggerated corkscrew pattern which does not resemble the general pattern of hyperplasia. There is then no evidence at present on this important point, and these cases must be further studied from this point of view.

A second important question arises: In these cases does the endometrium continue to undergo a cycle or is there a persistence of the secretory phase for a long period of time? If this latter possibility were correct, we would have a syndrome which might be comparable in its pathologic anatomy and physiology to endometrial hyperplasia. Unfortunately here too there is no conclusive evidence. However, from the material of this study, there is suggestive evidence which might support either point of view. Indeed there may be represented cases of each type.

The women complaining of simple menorrhagia, that is, those with increased menstrual flow with a normal interval and even those with a shortened interval, might be considered because of the regular periodic nature of their bleeding, to indicate a cyclic activity on the part of the endometrium. This is by no means certain, for periodic bleeding does not necessarily imply cyclic endometrial change. Martzloff, Novak and others have reported cases of endometrial hyperplasia with regular

normal periods. However, this is probably the exception rather than the rule and regular periodic bleeding most likely occurs more often from cyclic endometrium.

On the other hand, there are two points which might indicate that there is a persistence of secretory endometrium for a long period of time. First, there are 11 patients with a history of irregular bleeding obscuring the menstrual cycle. In 8 of these normal premenstrual endometrium was obtained from patients who had been bleeding for various lengths of time from twenty to thirty-four days. This may mean that the premenstrual endometrium had been present during the bleeding and perhaps even before, because in almost all patients there was a history of irregular menses immediately preceding the prolonged bleeding which was interrupted by the curettage.

Second, those patients with corpus luteum cysts may have had a persistence of secretory endometrium. It may be that these cysts secrete progesterone for a long period of time and thus maintain secretory endometrium. In such a case mentioned above, secretory endometrium was obtained after the cessation of a prolonged menstrual period.

It is possible to decide this important question of whether or not the endometrium continues to undergo its cycle by securing an endometrial biopsy once each week for several consecutive weeks. This can easily be done by an endometrial biopsy punch or a suction curette, taking care each time to secure a specimen of tissue from a different portion of the uterus. Such a series is now under consideration and will be reported in a later communication.

The fact that secretory endometrium is found in the presence of functional uterine bleeding might indicate that the fault lay in the function of the corpus luteum. The precise nature of this possibility is a matter of even greater speculation. Bleeding in the presence of progesterone might be considered to be at variance with the literature for Corner¹⁴ and others have demonstrated in the monkey that even small amounts of progesterone are effective in postponing the onset of an expected menstrual period and have shown that bleeding invariably occurs five or eight days after its withdrawal. Furthermore, it has been shown¹⁵ that progesterone is effective in preventing bleeding following the withdrawal of estrone and many authors have suggested its use in controlling functional uterine bleeding especially that associated with hyperplasia. However, it might be possible that prolonged bleeding from secretory endometrium would occur if progesterone were gradually withdrawn. This possibility also does not seem to be likely, for Hartman and Markee¹⁶ in work which has not yet been published have shown in the monkey that bleeding does not occur under these conditions and have demonstrated that the endometrium undergoes an involution without shedding or bleeding. The unraveling of this conflict must await future observations. However, the conflict may be more apparent than

real for, although we know that bleeding will occur following the withdrawal of esterone and progesterone, we do not know if this is the important factor in bleeding or whether this is but a link in a much more complex chain. There might even be some positive factor in bleeding having no direct relation to the phase of the endometrium as was suggested by the work of Hartman, Firor and Geiling¹⁷ and recently championed by Wilson and Kurzrok.¹⁸

It seems clear that functional uterine bleeding can be associated with secretory endometrium, and it may be possible that, in at least some cases, there may be a persistence of secretory endometrium for a long period of time.

SUMMARY

1. It has been too widely accepted that functional uterine bleeding is almost invariably associated with endometrial hyperplasia, but in our experience with 83 consecutive cases about 14 per cent are associated with secretory endometrium.

2. Forty-one cases of functional uterine bleeding associated with secretory endometrium are studied in detail. (a) In most cases the complaint was simple menorrhagia. (b) Secretory endometrium was found during bleeding which lasted for as long as thirty-four days, and it was also found after prolonged bleeding associated with corpus luteum cysts, suggesting the possibility that with functional uterine bleeding secretory endometrium may persist for a long period of time.

NOTE: I wish to express my appreciation to Dr. Thomas S. Cullen, Dr. Carl G. Hartman, and Dr. Richard TeLinde for many valuable suggestions in the preparation of this report.

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BIOLOGY OF THE HUMAN VAGINA IN PREGNANCY*

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THE investigations of Hitschmann and Adler established the cyclical changes in the uterine endometrium and initiated a field of research which has yielded rich rewards. In the years that followed the observations of these authors numerous contributions have established the ovarian-uterine relationship. Attention has been focused on the kaleidoscopic changes in the uterine endometrium because of their magnitude and because menstruation, a signal event in the life of woman, heralds the termination of the cycle. It is only within recent years that the other derivatives of the müllerian system have been thoroughly investigated.

Wollner recently demonstrated cyclical changes in the cervical mucosa. The fallopian tubes and the vagina are likewise derivatives of the müllerian system. Seckinger and Snyder noted that spontaneous contractions of the fallopian tubes became more marked and rapid following ovulation and that this activity was greatly diminished during pregnancy. The recent work of Robert Meyer and Kóff agreed on the fact that all of the vagina except the very distal portion is undoubtedly of müllerian origin. Thus the vaginal mucosa throughout most of its extent should be under the same influences as the uterine endometrium.

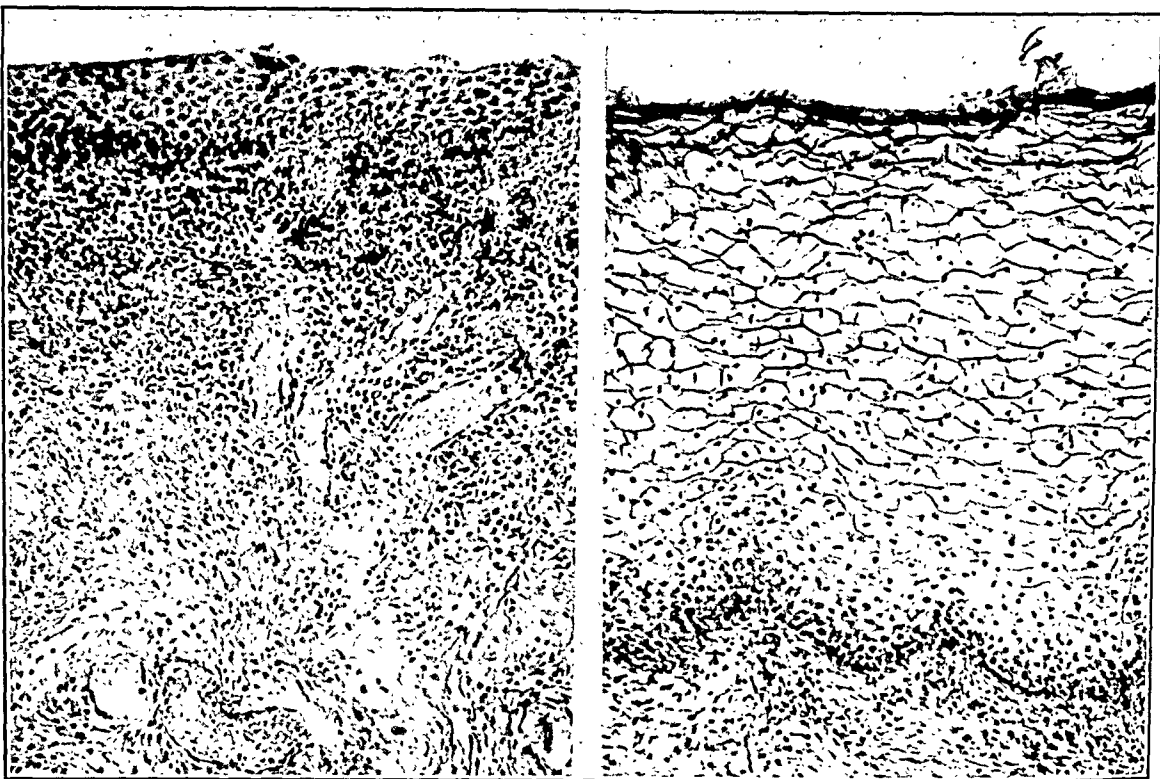
Study of the vaginal mucosa was given impetus by the work of Stockard and Papanicolaou who in 1917 introduced the vaginal smear method of following the sexual cycle in experimental animals. Daily vaginal smears in rodents give an accurate picture of the cyclical changes in these animals in that they reflect the changes in the vaginal mucosa. These basic experiments provided the test animals necessary for the rapid development of our knowledge concerning the endocrine glands associated with the sexual cycle.

The great difficulty in obtaining suitable human material and the absence of marked changes resulted in a variation of experimental results when the human mucosa was first studied. Thus Stieve in 1925 concluded that there were no regular cyclical changes in the human vagina in the nonpregnant individual. However, he described many changes during pregnancy resulting in a tremendous thickening of

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the vaginal mucosa. The loss of a good portion of this epithelium following parturition he ascribed to mechanical factors incident to delivery, such as stretching and trauma resulting in infection. As recently as 1936, Zondek and Friedmann questioned the ovarian control of the vaginal mucosa in the human in spite of the increasing amount of experimental evidence to confirm it.

Dierks and Puccioni in 1927 independently studied the vaginal mucosa in the human using suitable material and came to similar conclusions. They described characteristic histologic changes accurately correlated with the menstrual cycle. Their material was adequate and well controlled, thus establishing the existence of a vaginal cycle dependent on ovarian activity.



A. (H. and E.)

B. (H. and E.)

Fig. 1.—H. and E. (160X.) (A) Biopsy from the vagina of a patient in the late postmenopausal period. The squamous epithelium is very low, consisting of four or five layers of cells. The individual cells are small, indistinct with opaque cytoplasm and dark staining nuclei. The basal layer of cells is irregular and devoid of a distinct basement membrane. There is a lack of cellular activity. (B) Biopsy from the vagina of the same patient taken after three weeks' treatment with estrogenic hormone. Note the marked proliferation of the squamous epithelium. The basal cells are regular, show marked activity. Most of the thickness of the epithelium is the result of many layers of large, discrete, vacuolated appearing cells. The uppermost layer or functionalis consists of desquamating, flattened cells. This is the characteristic histologic picture of a patient in the active sex years.

Davis and Hartman in 1935 carefully reviewed the work that preceded in an attempt to evaluate its significance. The primates are the only animals which menstruate. To determine the presence of a vaginal cycle in primates the authors began an investigation of a large series of monkeys in the Carnegie colony. Weekly biopsies of the vagina were made and the findings carefully correlated with vaginal smears and cyclical events in the ovaries. Their conclusions were that the vagina of the monkey undergoes cyclical changes perfectly coordinated with ovarian activity and ovulation. The next year Traut, Block and Kuder at Cornell University

confirmed these findings in the human species thus affirming the fact that in woman as in her near-kin, the higher apes, cyclical activity occurs in the vaginal epithelium.

Following up the experimental work on the monkey, Davis in 1935 reported an extensive study on the postmenopausal changes in the vaginal mucosa as a result of the normal or an artificial climacteric. He found that the squamous epithelium undergoes slow atrophy, the cells become smaller, the nuclei pyknotic. The basal layer of cells becomes inactive and loses its normal, smooth alignment on the basement membrane. The functionalis is lost and no cyclical activity can be seen. The thin, glistening, parchment-like mucosa, when subjected to even mild trauma, becomes damaged and if infection occurs it results in the clinical condition described as senile vaginitis. Upon the administration of estrogenic hormone in the form of suppositories or hypodermically, the senile vaginal mucosa undergoes a marked awakening. It becomes thicker, more velvety to the touch, pinker and now resembles the vagina of the young woman. Biopsies reveal a tremendous proliferation of the basal cells, the development of a thick basalis as well as a functionalis.

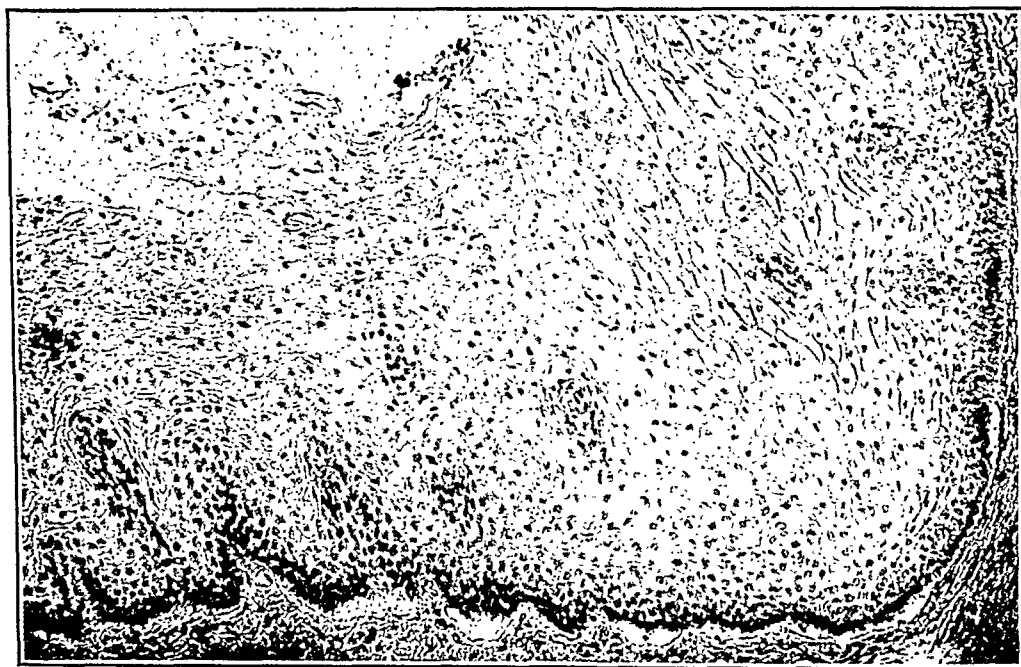


Fig. 2.—H. and E. (160X.) A section of the squamous epithelium of the vagina of a newborn baby. Note that it consists of many layers of large, clear cells with small nuclei. These cells are rich in glycogen. The basal cells are active consisting of several layers.

Microscopically, these changes are astounding as one can see from the photomicrographs (Fig. 1). These proliferative changes reach a maximum in ten days or two weeks and will remain thus as long as the estrogenic hormone is administered, but at its withdrawal retrogressive changes set in to continue until the vaginal mucosa has returned to its normal postmenopausal state. These experiments have resulted in a rational treatment for senile vaginitis which has stood the test of time.

Lewis, in 1933, following the experimental work of Corner and Allen on immature monkeys, described a treatment for gonorrheal vaginitis in children based on physiologic changes in the vagina which he had observed. The immature type of squamous epithelium of the vagina could be rapidly converted into the adult type by the use of estrogenic hormone. This adult type of vaginal epithelium with its abundance of glycogen usually results in the production of a marked vaginal acidity. This unfavorable reaction and the thickened adult type of epithelium are inimical to gonococci and they usually disappear.

Cruickshank and Sharman in 1934 reported careful studies on the histologic appearance of the vaginal mucosa in fetuses, infants, prepubertal and postpubertal children, and sex mature women. These can be briefly summarized. During intrauterine life, after the development of the epithelial covering of the vaginal lumen, it consists of twenty to thirty layers of large vacuolated cells with an active basal layer. In every way this epithelium resembles that seen during the active sex years (Fig. 2). Following delivery this epithelium becomes progressively thinner, the individual cells smaller, the basal cells less and less active. Within a month of extrauterine life the epithelium reaches its lowest ebb, consisting of several layers of small inactive cells (Fig. 3). This inactive epithelium remains unchanged during the developmental years of the growing girl until the onset of puberty and the initiation of hormone activity cause a rapid reawakening of the dormant epithelium. The mucosa becomes thicker, pinker, and more velvety to the touch. The basal layer of cells begins a rapid proliferation and the marked activity



A. (H. and E.)

B. (Best's carmine)

Fig. 3.—(A) A section of the vaginal mucosa of an infant three months old. The squamous epithelium consists of three or four layers of small cells entirely inactive. This epithelium resembles that seen in the postmenopausal period. In both instances there is an absence of estrogenic hormone. (B) The same section stained for glycogen and showing its complete absence.

here is evidenced by the numerous mitoses. Twenty or thirty layers of cells are rapidly built up and the mucosa assumes the florid appearance of that of the mature woman, to remain thus until the cessation of ovarian function.

THE RÔLE OF GLYCOGEN IN THE VAGINAL EPITHELIUM

The presence of glycogen in the vaginal epithelium has been known for a long time. When present it is chiefly confined to the cells although the interstices also appear to contain it. Within the cell walls glycogen appears in the form of granules concentrated chiefly about the periphery of the cells. This granular form is not an artifact due

to tissue fixation for this characteristic distribution was retained when tissues were carefully fixed by the Altman freezing-drying technique of Gersh and Bensley, in which normal cell relationships are retained. The basal layers of actively proliferating cells contain no glycogen which is chiefly concentrated in the uppermost two-thirds of the epithelium. The large vacuolated cells which appear in hematoxylin-eosin stained sections contain the most abundant glycogen. As the cells reach the surface, become flattened and are about to be desquamated they still contain considerable glycogen.

The important rôle of glycogen in maintaining a normal vaginal acidity and a resultant normal flora was described by Krönig and Menge in 1897. These and subsequent workers realized that glycogen had to be converted into utilizable carbohydrates so that it could be attacked by vaginal bacteria and converted into lactic acid. Although the exact chemical process involved in this biologic mechanism is not definitely known, it is thought that glycogen is broken down by nonbacterial enzymes into a stage in which it can be attacked by bacteria. These organisms, largely Döderlein's bacilli, convert these utilizable sugars into lactic acid. These bacteria, because of their acid-resistance, are largely responsible for the high degree of acidity produced in the vagina which normally reaches pH 5.7 to 4.8 (Fig. 4). Possibly under certain circumstances Döderlein's bacillus can ferment glycogen directly into lactic acid.

Miura, in 1928, again drew attention to the presence of glycogen in the vagina, and from a large series of observations he concluded that there existed an intimate relation between the deposition of glycogen and ovarian activity as indicated by cyclical events, such as ovulation and menstruation. Cruickshank and Sharman in an extensive series of experiments and observations elucidated the facts concerning the biology of the vagina in the human subject. These workers corroborated many known facts and added new ones to explain the intricate mechanism present in the human to maintain normal biologic relationships.

The glycogen content of the vagina is dependent on the character of the epithelium which in turn is under the influence of estrogenic hormone, the result of ovarian activity. Thus the presence of glycogen has been demonstrated in the vagina of the fetus in the late prenatal period and in the newborn. The estrogenic stimulation to the vaginal epithelium probably is maternal in origin for within several weeks after birth the vaginal mucosa rapidly disintegrates resulting in an epithelium of several cells in thickness devoid of glycogen. This epithelium does not change throughout the developmental years of the girl until the onset of pubertal changes. The epithelium is built up to many layers of cells and an abundance of glycogen fills these cells. Soeken described abrupt changes in the vaginal acidity and flora associated with this change in the character of the epithelium of the vagina. These changes are brought on by the initiation of ovarian

activity and resultant cyclical changes. With the cessation of ovarian activity at the menopause, whether normal or artificially induced, the epithelium slowly reverts to six to ten layers of small, compact, rela-

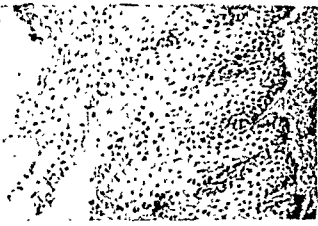


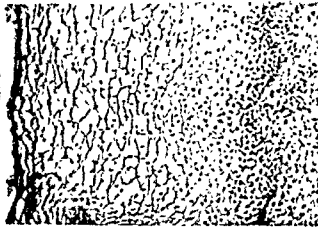
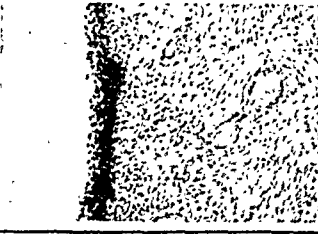
Estrogenic hormone	Newborn	Month old Child	Puberty	Sex-Mature	Post-Menopause
	+	—	appears	+	—
Epithelium					
Glycogen	+	—	— to +	+	—
	acid pH 4-5	alkaline pH 7	alkaline ↓ acid	acid pH 4-5	neutral or alkaline pH 6-7
Flora	sterile → Döderlein's bac. (secretion abundant)	sparse, coccal and varied flora (secretion scant)	sparse, coccal ↓ rich bacillary	Döderlein's bacilli (secretion abundant)	varied flora (secretion scant)

Fig. 4.—This figure illustrates the dominant rôle of estrogen in the control of the biology of the vagina and of the character of its mucosa.

tively inactive cells, devoid of glycogen. Thus, the presence of glycogen in vaginal epithelium is dependent on an active, proliferating, many layered, sex-mature type of epithelium which in turn is dependent on estrogenic hormone (Figs. 5 and 6).

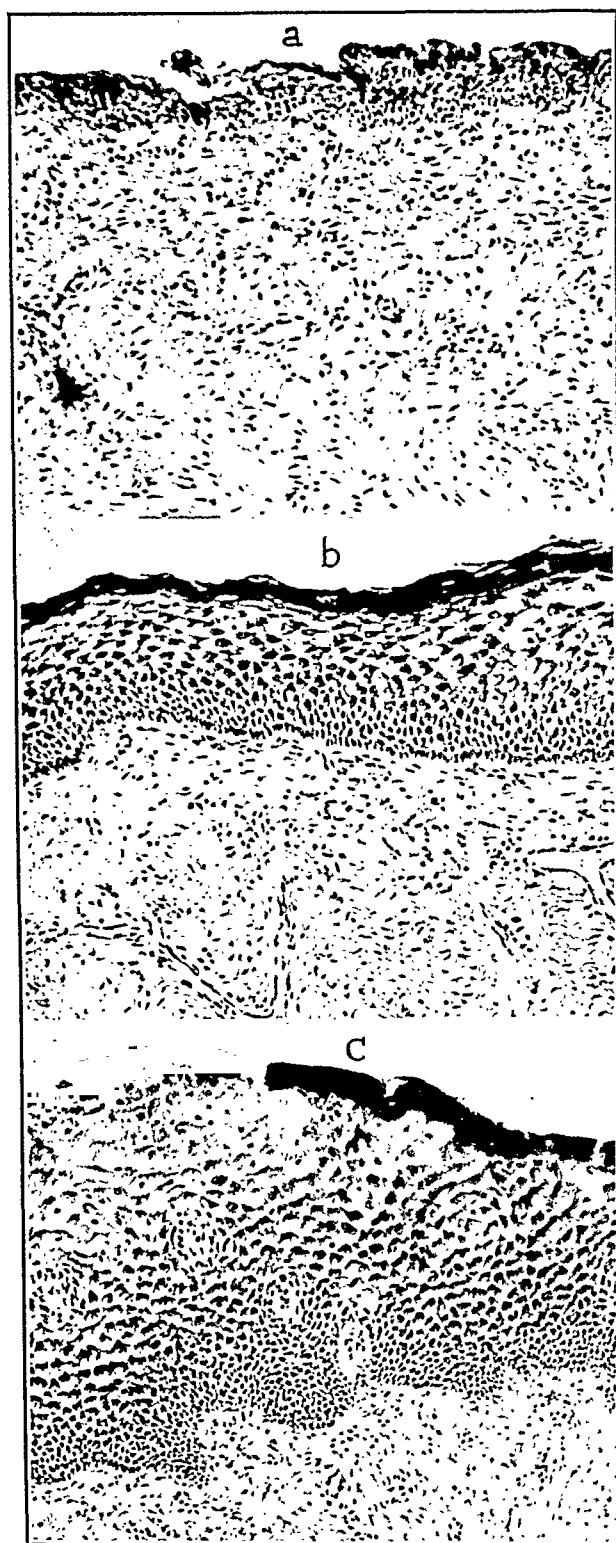


Fig. 5.—Sections stained with Best's carmine. (160 \times .) (A) Typical atrophic squamous epithelium of the postmenopausal period. (B and C) Two and four weeks following the administration of estrogenic hormone. Note the progressive increase in thickness of the epithelium and the marked deposition of glycogen in the vacuolated appearing cells. Note likewise the well developed functional layer which stains black as a result of the accumulation of glycogen in the flattened cornified cells of this layer.

PRESENT MATERIAL

This study was conducted along the same lines described in previous papers published by the author. Biopsies were obtained at two and three weekly intervals from the vaginas of a group of normal pregnant women throughout their pregnancies and for at least three months postpartum. Suitable biopsies can be readily obtained by means of a small punch previously described. As a rule a small amount of novocaine is infiltrated beneath the site to be biopsied, thereby raising the vaginal mucosa as a bleb, facilitating the removal of the biopsy specimen. There is little or no pain associated with this simple procedure even though no local anesthesia is used. Smears and cultures were taken prior to each biopsy removal.

The specimens were removed from the same portion of the vaginal wall so that comparative results would be more significant. The site

Mechanism for Maintenance of Normal Vaginal Acidity

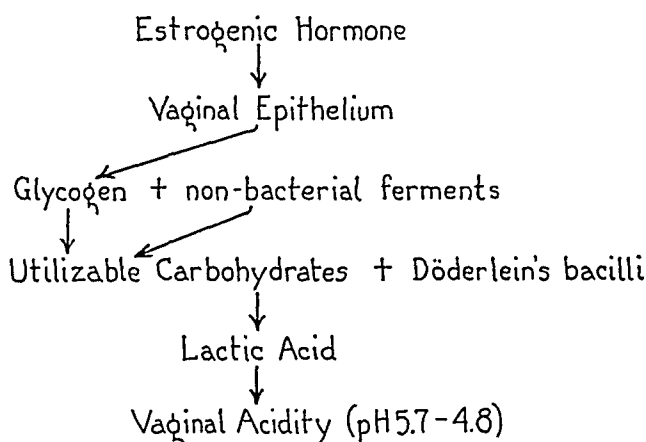


Fig. 6.

selected was the lateral wall approximately six or seven centimeters from the introitus, in the upper third of the vagina. A previous study had demonstrated some slight variation of the thickness of the mucosa in the several parts of the vagina but these were of no appreciable significance. The tissue was immediately cut into two portions, one of which was fixed in absolute alcohol for glycogen studies, the other in Bouin's solution for histologic studies.

Gross changes in the vaginal mucosa became evident as the pregnancy advanced. The increasing vascularity occasionally resulted in some bleeding but this was easily controlled by a small tampon which was left in situ for several hours. A sharp punch will remove an uninjured piece of mucosa with its underlying tunica propria, thereby safeguarding normal relationships.

After fixation the specimens were carefully embedded in paraffin using a magnifying lens to assure a perfect lateral section. They were

cut about 5 microns in thickness and stained by hematoxylin and eosin. Special stains were used to study minute histologic features.

Best's carmine stain was used for the glycogen studies. This process stains the nuclei and cytoplasm of the cells a pale blue and the glycogen red. The efficacy of the stain and method was carefully controlled by using the method of Russell. He found that glycogen is dissolved by diastase in the saliva so that the former can be washed off in water whereupon when the section is stained by Best's method glycogen is absent in this control section. Some of the sections were counter-stained by hematoxylin and eosin to accentuate the cytology.

We began our study on thirty normal women, the majority of which were primiparas. As the study progressed four of these women were dropped from observation due to premature termination of their pregnancies or to their failure to continue at the clinic. In two other women, regular biopsies could not be taken so that these were likewise discarded from this study. It was possible, therefore, to obtain regular biopsies during pregnancy, parturition and for three months postpartum on a group of 24 women (Table I). In a number of these women it was possible to obtain 15 biopsy specimens. These histologic studies were carefully correlated with studies of the cellular and bacteriologic content of the vaginal lumen. Papanicolaou has amply demonstrated that studies of the cellular content of the vaginal lumen in the human reflect accurately the changes taking place in the vaginal mucosa for the former is the result of the latter.

The deliveries of these women were accomplished in a number of ways. The majority delivered normally, the primiparas with the aid of an episiotomy. Some were delivered by the forceps operation. In two instances, fortunately for this study, elective cesarean section terminated the pregnancy. A number of possible candidates for this operation were purposely picked for the study. Stieve was so impressed by the traumatic factor in the postpartum changes in the vaginal mucosa that the elimination of all trauma of labor was desirable in a few cases in our series in order to evaluate their importance. One of our patients delivered twins near term. The reestablishment of menses in the postpartum period was noted in an attempt to correlate ovarian function and a return of cyclical changes in the vagina. Other than these facts, there was little in the clinical histories of the group of patients which would be pertinent to the present study.

PREGNANCY CHANGES

Davis and Hartman in 1935 reported the results of a study on the changes in the vaginal epithelium during pregnancy and the puerperium in a series of Rhesus monkeys of the Carnegie colony. These observations in many ways closely resemble the changes to be de-

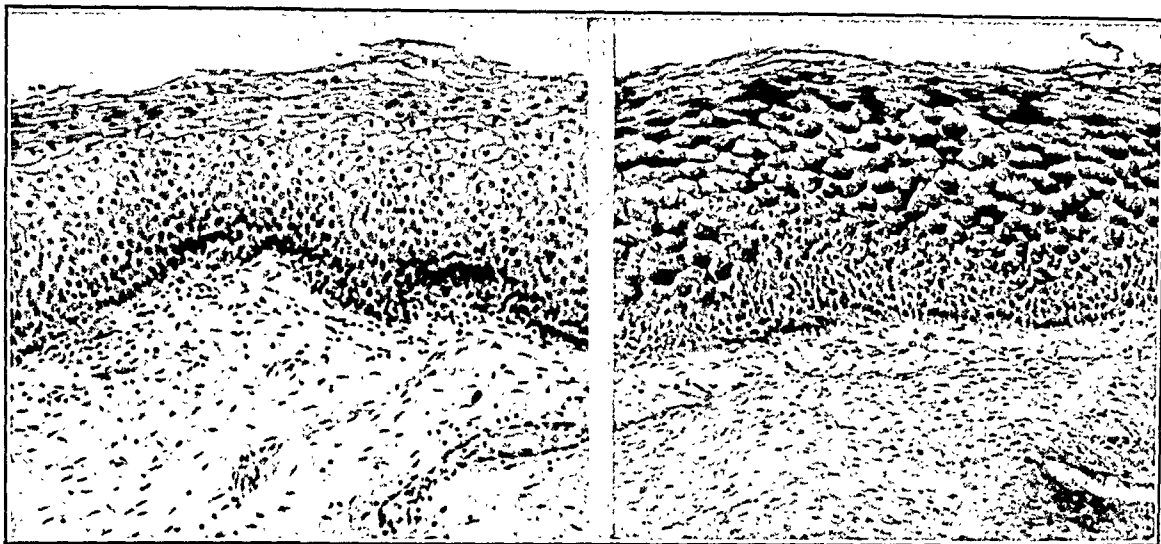
scribed in the human female. This is not a surprising fact for this experimental animal and the human female are the only primates who exhibit cyclical and endometrial changes eventuating in menstruation. Furthermore, these primates are the only species in which glycogen is present in the vagina. Thus, it would appear that the physiologic changes in the genital tract should be analogous.

The vaginal epithelium as early as the twelfth week of gestation shows marked thickening, reaching a thickness of 500 microns near the end of gestation. An active proliferation of the basal cells can be seen, and four or five layers of actively dividing cells constitute the basal portion of the epithelium. Numerous mitotic figures bear evi-



Fig. 7.—This is a high power of the superficial portion of the functional layer showing the desquamation of the cells. Note how they literally crumble away from the surface. These cells, although distinctly necrotic, still contain an abundance of glycogen.

dence of this active cell division. Above these actively proliferating cells one can count 20 to 30 layers of large vacuolated-appearing cells in which the nuclei stand out prominently. These cells are normally laden with glycogen and the vacuolization is in part the result of a disappearance of glycogen in the fixation of the tissue. The uppermost layer or functionalis consists of cells from the lower layers which have worked upward. They have become flattened and compressed but still contain an abundance of glycogen in their cytoplasm. The superficial cells of this layer are continually breaking away from their attachment (Fig. 7). This extensive desquamation provides the profuse

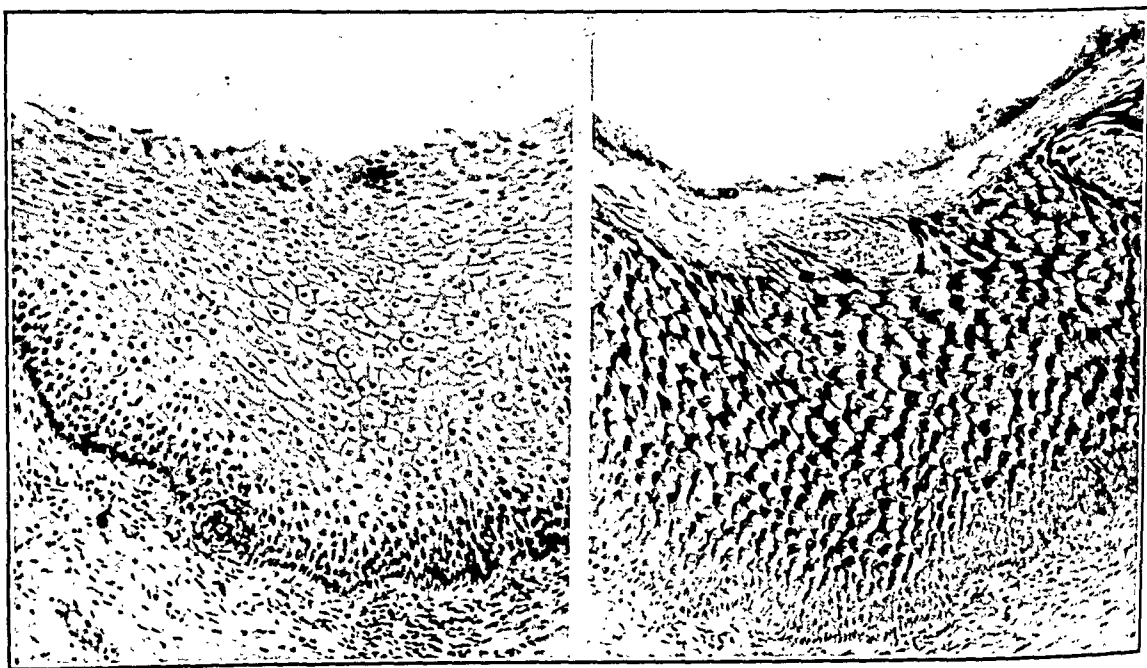


A. (H. and E.)

B. (Best's carmine)

Fig. 8.—This is the first of a series of five sections taken during various periods of pregnancy and stained with hematoxylin-eosin and Best's carmine for glycogen. They are all of the same magnification (160X) and therefore provide a good comparison as to the thickness of the epithelium and the changes in its cellular structure.

Biopsies taken at eleven weeks' gestation. (A) This section shows the epithelium of moderate thickness. The basal layer consists of three or four layers of cells in which there are signs of cellular activity. The functional layer stands out distinctly. (B) In this glycogen preparation one can note that the middle layers of cells which appear in the previous section as vacuolated contain an abundance of glycogen. There is, however, an absence of glycogen in the three or four layers of active basal cells. The functionalis likewise contains considerable glycogen.



A. (H. and E.)

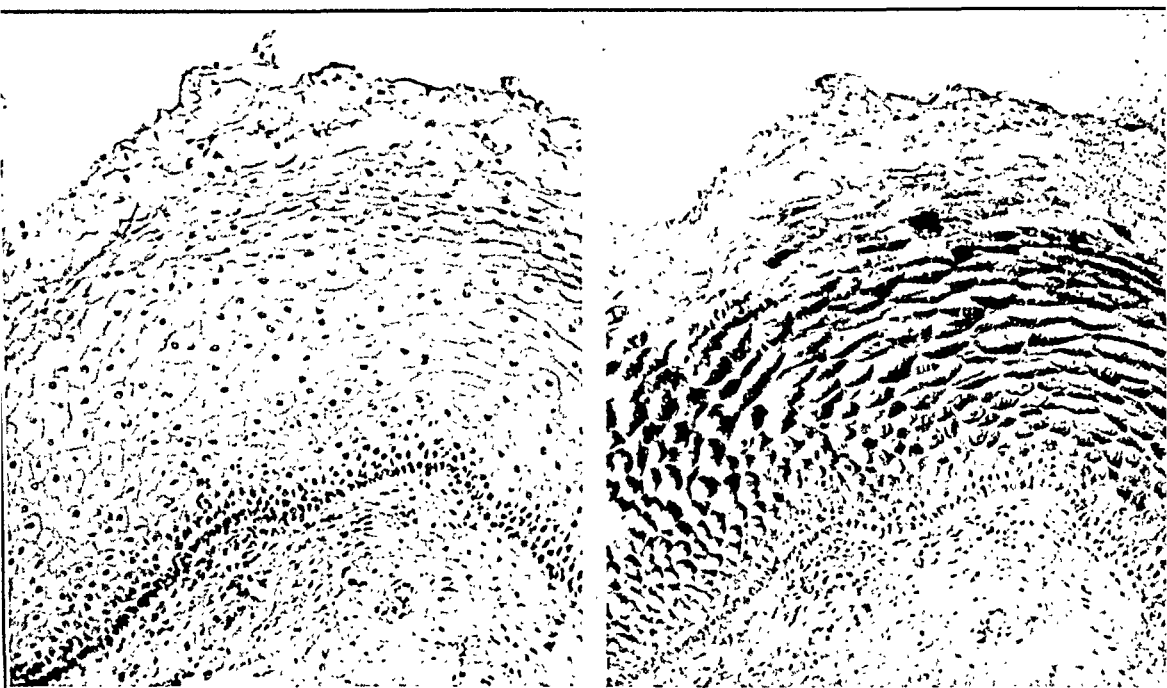
B. (Best's carmine)

Fig. 9.—Biopsies taken at fourteen weeks' gestation. (A) This section shows the progressive increase in the thickness of the epithelium as well as in the activity of the basal cells. (B) The glycogen can be seen in these cells in the form of granules surrounding the nucleus.

characteristic secretion in the vaginal lumen as well as the glycogen necessary for the maintenance of the vaginal acidity (Figs. 8 through 12).

In the functionalis one can see large abnormal appearing cells, some round or oval, others oyster-shaped with large round nuclei. These cells probably represent the so-called "pregnancy cells" which Papanicolaou has described in the cellular content of the vaginal lumen during pregnancy.

The maximum proliferation and development of the vaginal mucosa is probably reached at mid pregnancy and this condition is maintained until near the end of gestation. There is some variation in different



A. (H. and E.)

B. (Best's carmine)

Fig. 10.—Biopsies taken at twenty-two weeks' gestation. (A) Except for the increase in the thickness of the epithelium there is little change from the previous section. (B) Histologically there appears to be a distinct increase in the amount of glycogen in the individual cells. Note likewise the increased thickness of the desquamating layer.

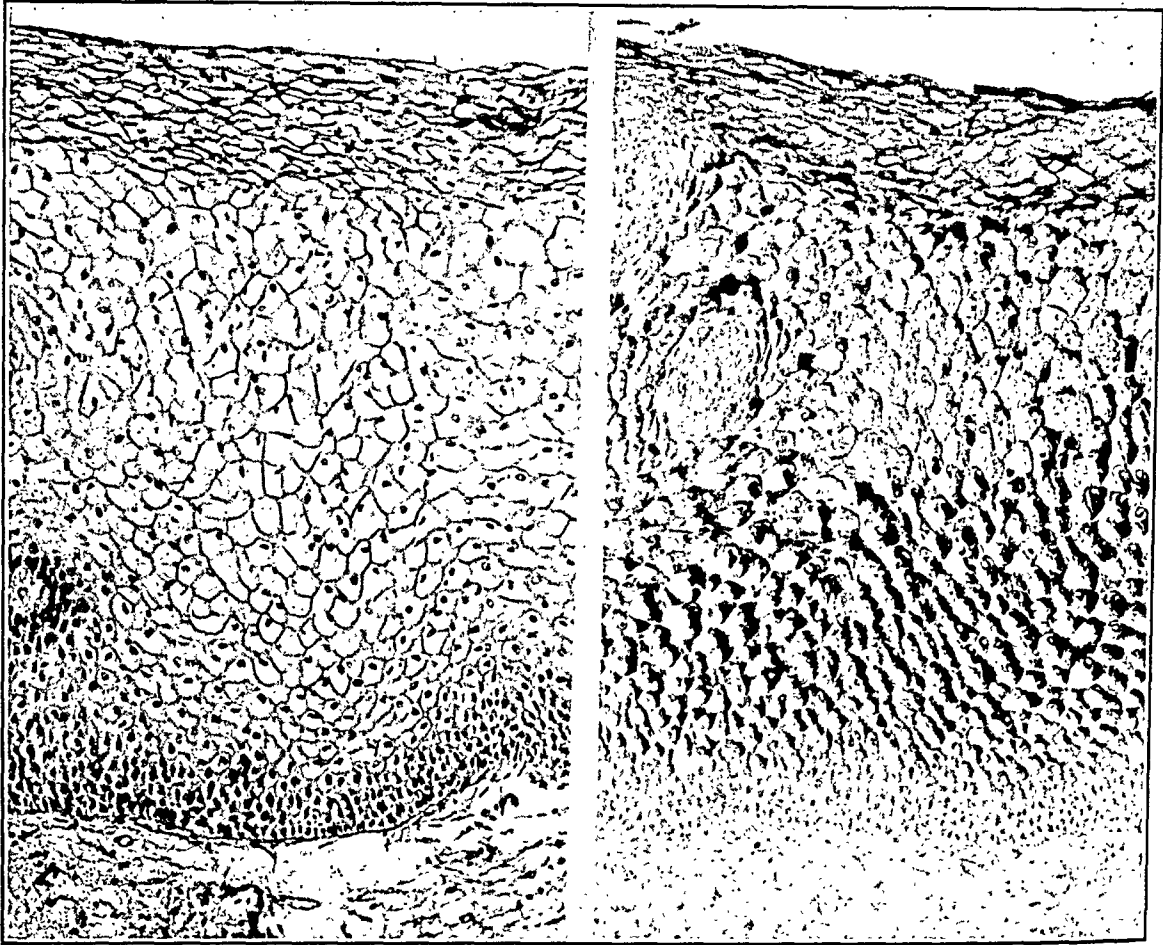
individuals so that the cellular development is greater in some than in others. However, one can follow the changes described in all the normal gestations.

As term approaches one notes a diminution in the thickness of the vaginal epithelium in a majority of the patients. This is not as marked as in the case of the monkey but nevertheless the change in the epithelium is sufficient to be noted. The cells still contain an abundance of glycogen but there is considerably less activity in the basal cells than was evident in early gestation.

The profuse, creamy, whitish secretion of normal pregnancy consists largely of desquamated epithelial cells, cervical mucus and Döderlein's

bacilli. The amount of this secretion increases as pregnancy advances. This increased amount is largely due to the cytologic activity of the vaginal epithelium. The reaction is acid and Miura has estimated that the amount of titrable lactic acid increases from 0.4 per cent early in pregnancy to 0.9 per cent by the end of pregnancy.

Following the birth of the baby marked retrogressive changes rapidly manifest themselves in the vaginal mucosa. It becomes progressively thinner so that at the end of two weeks the entire thickness

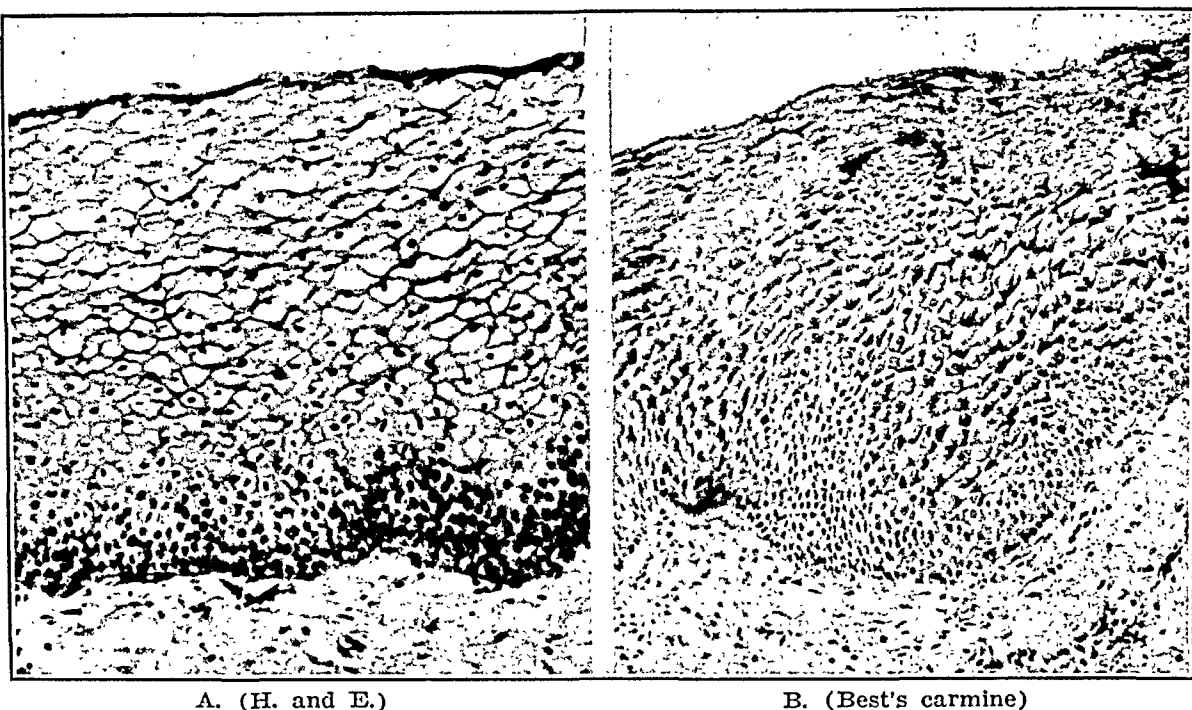


A. (H. and E.)

B. (Best's carmine)

Fig. 11.—Biopsies taken at thirty-six weeks' gestation. (A) The thickness of the epithelium has apparently reached the maximum although there seems to be less activity in the basal layer of cells. Note particularly the rather marked differentiation of the epithelium into its various component parts. (B) The distribution and character of the glycogen in the large vacuolated cells is particularly well demonstrated in this section.

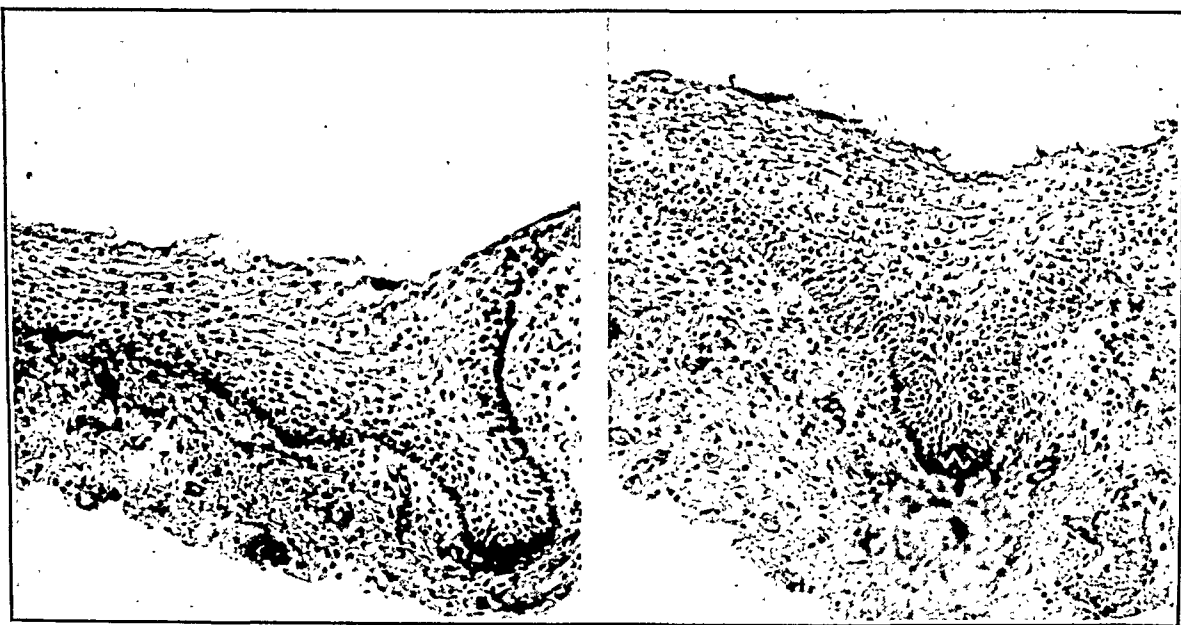
may comprise six to ten layers of cells. The basal cells consist of a single layer of small cells, somewhat irregularly arranged on the basement membrane. The normal orderly alignment of discrete cuboidal cells on a clean cut basement membrane present prior to delivery is missing. The individual cells are small, with dark nuclei and show no evidences of cellular activity. The remaining cells likewise have become smaller, more compressed and irregularly arranged. Gone are



A. (H. and E.)

B. (Best's carmine)

Fig. 12.—Biopsies taken at thirty-eight weeks' gestation. (A) At term there appears to be a decrease in the thickness of the epithelium as well as a diminution in its activity. This is not a consistent finding but it is very common. (B) There likewise appears to be a diminution in the amount of glycogen present at this period of the gestation.



A. (H. and E.)

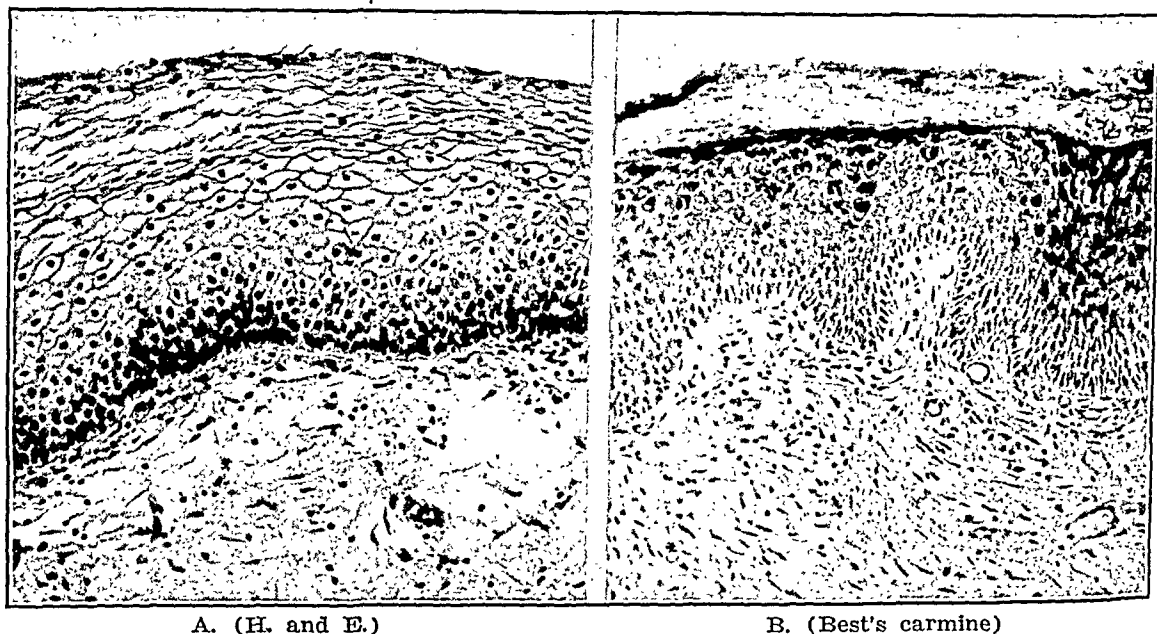
B. (Best's carmine)

Fig. 13.—This is the first of a series of three sections taken during the postpartum period in the same patient. They are all of the same magnification (160X) and therefore provide a good comparison as to the thickness of the epithelium and the changes in its cellular structure.

Biopsies taken at eight days postpartum. (A) Note the marked decrease in the thickness of the squamous epithelium. A large portion of it has been lost by desquamation. The individual cells are small and appear distinctly inactive. The large vacuolated cells of the pregnancy period have disappeared. (B) This section stained for glycogen shows its total absence.

the large, clear cells which formerly were filled with glycogen and the functionalis with the desquamating epithelial cells. In fact the epithelium has reverted to the type almost characteristic in the post-menopausal period, inactive and devoid of glycogen (Fig. 13).

The extent of the destructive processes described varies considerably in different individuals but the general picture is present in all. The absence of glycogen in the cells is particularly significant. That these changes are not the result of changes incident to the trauma of labor itself is evident from the fact that the type of delivery does not affect the subsequent changes in the vaginal mucosa. The patients delivered by cesarean section where no vaginal trauma has taken place exhibit similar changes.



A. (H. and E.)

B. (Best's carmine)

Fig. 14.—Biopsies taken at five weeks postpartum. (A) The squamous epithelium is again proliferating. This is best seen in the basal layer which consists of three or four layers of active cells. A functional layer is likewise developing. (B) In the glycogen preparation one notes particularly the recurrence of glycogen in the vacuolated cells as well as in the desquamating cells of the functionalis.

Unfortunately, the vaginal secretion and possible changes in the vaginal flora cannot be studied during the puerperium for lochial discharges resulting from uterine involution completely obscure any vaginal findings.

Four to six weeks postpartum the epithelium begins to show signs of proliferative activity (Figs. 14 and 15). This is first apparent in the basal layers of cells in which cell division and growth are manifest. Soon three or four layers of cells comprise this layer. These cells are packed close together. They contain little cytoplasm and their nuclei stain darkly and contain numerous mitoses. The epithelium grows in thickness by a rapid increase of large, vacuolated appearing cells

which are filled with glycogen. Finally, the functionalis appears and the flattened, nonnucleated, glycogen containing cells begin to crumble away from the surface of this layer. Usually the vaginal mucosa is completely restored within six or eight weeks following childbirth. The recurrence of the menses is usually indicative of renewed cyclical activity although the vaginal mucosa is most often completely restored before the menses are reestablished.

Following gestation there is an immediate and rapid drop in the estrogenic level in the blood and urine of the patient. This results in

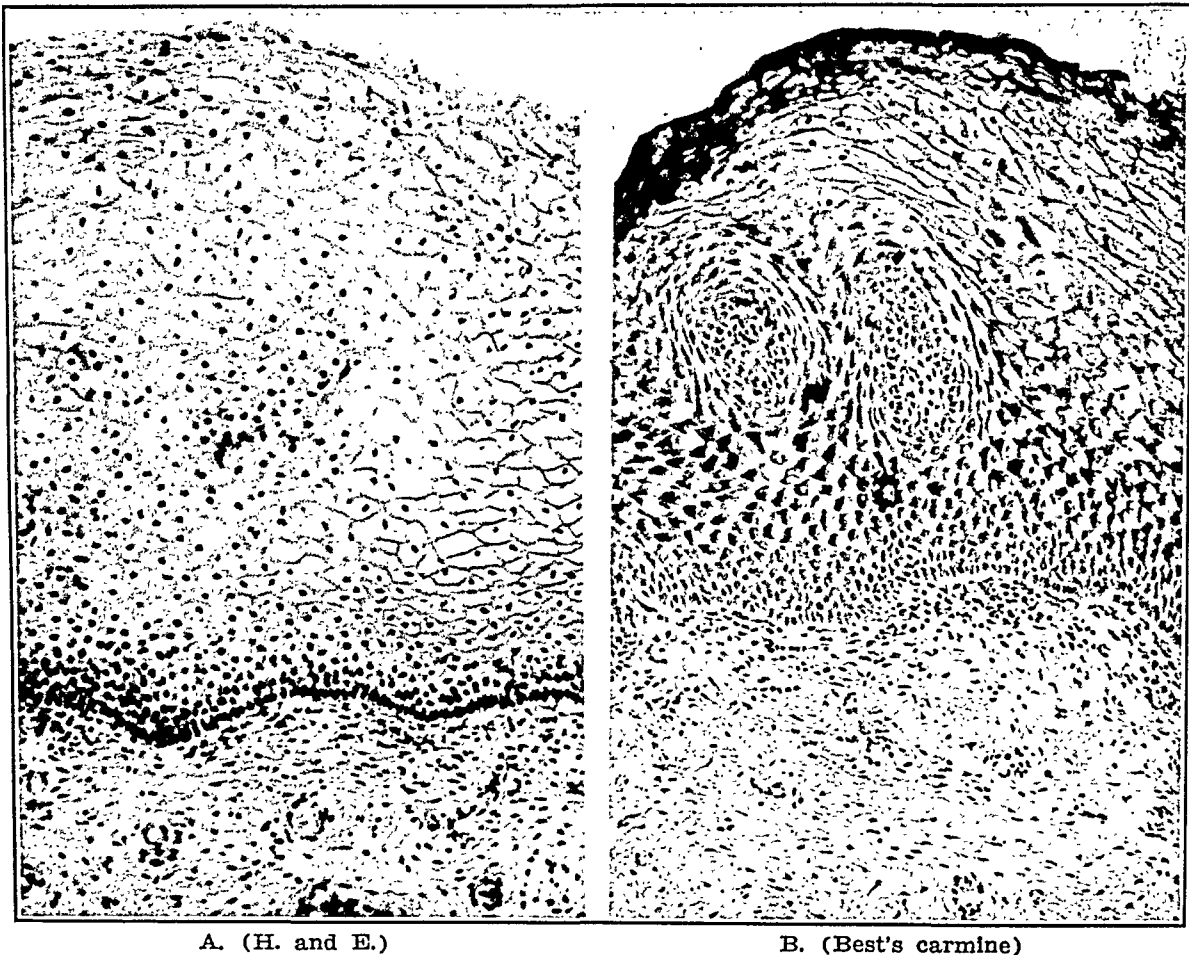


Fig. 15.—Biopsies taken at nine weeks postpartum. (A) The vaginal mucosa has not completely recovered following the reestablishment of cyclical activity in the ovary. (B) Note the characteristic glycogen distribution is once again manifest.

a rapid retrogression on the part of the vaginal epithelium. It becomes thinner, the cells smaller and inactive. Glycogen entirely disappears from the cells. Undoubtedly the vaginal secretion changes and the acidity disappears but these changes are masked by the profuse bloody uterine discharge. The epithelium remains in this inactive state until the initiation of follicle activity in the ovary results in a reestablishment of cyclical activity in the genital tract.

The changes in the vaginal mucosa that result from pregnancy and parturition are entirely under estrogenic control. These observations

confirm the rôle of estrin in the maintenance of biologic relationships in the vagina. During pregnancy there is present an excessive production of this hormone and a marked increased concentration in the blood. Just where it is produced is still questionable. Under the influence of this abundant hormone, the vaginal mucosa undergoes its most marked proliferation. The cells become large and filled with glycogen. The increased activity on the part of the epithelium results in an excessive desquamation of cells from the thickened functionalis. These desquamating cells, rich in glycogen, result in a profuse characteristic, highly acid, vaginal secretion. Döderlein's bacilli in almost a pure culture provide the ideal flora necessary to maintain this vaginal acidity or thrive because of it.

DISCUSSION

The intricate mechanism for the control of biologic relationships in the vaginal tract is the result of morphologic changes in the vaginal epithelium, chemical changes and bacterial flora. Thus, the flora is dependent on the vaginal acidity, the vaginal acidity is the result of the action of enzymes on the glycogen, and the presence of glycogen is dependent on an actively proliferating epithelium. The latter is under the influence of estrin. These factors are therefore all under ovarian control. During pregnancy and parturition these are still under estrogenic control although the source of this hormone is not definitely known. Disturbances of any of them may easily upset the delicate balance, resulting in pathologic consequences.

These basic facts just described provide a logical explanation of the causation and therapy of many clinical conditions. Suffice it here to touch on a few of these. Yeast vaginitis is a particularly troublesome infection of the lower genital tract that occurs most often during pregnancy. It is almost impossible to eradicate this condition during pregnancy and the symptoms are difficult to control. Following parturition the infection disappears without treatment, occasionally to recur at a later date. Pregnancy provides an ideal opportunity for a yeast infection of the vagina, for the abundance of glycogen in the vaginal mucosa results in an ample supply of utilizable sugars and an acid medium. Both of these factors are necessary for the growth of yeast cells, so that if these organisms are present in or are introduced into the vagina, pregnancy offers the ideal conditions for their growth. Following delivery, the retrogression of the vaginal epithelium and the disappearance of glycogen remove the necessary factors so that the fungi quickly disappear and the patient is cured of her vaginitis.

The author has seen three cases of gonorrheal infection in the lower genital tract in the late postmenopausal period. The infection here

as in childhood selects as the site of predilection the vaginal mucosa. The atrophic, senile vaginal epithelium is no defense against the gonococcal penetration and the absence of glycogen with the resultant alkaline reaction of the scant secretion offers a favorable medium for these organisms. The resulting infection is predominantly a vaginitis. The only treatment used was estrogenic hormone in the form of vaginal suppositories, and the rapidity of disappearance of symptoms and organisms was astounding. Within ten days these patients were symptom-free and had negative smears. The senile, atrophic mucosa was replaced by an active, proliferating epithelium of the sex-mature type.

The rational treatment of senile vaginitis and gonorrheal vaginitis in children has been previously alluded to. These examples should lead to continued advances in rationalizing the treatment of lower genital tract infections.

Papanicolaou in 1933 suggested that smears of the cellular contents of the human vaginal lumen would reveal the character of the cyclical changes in the ovary. Furthermore, pregnancy resulted in a typical vaginal smear of considerable diagnostic importance. Smith and Brunner have just published the results of their study on the use of vaginal biopsies in the diagnosis of pregnancy. Papanicolaou and Shorr recently demonstrated the value of the vaginal smear as an index of the action of ovarian follicular hormone in the therapy of the menopause and endocrine disturbances.

Lastly, the intricate biologic mechanism for the control of vaginal acidity must have many important functions. Certainly it is not bold to imagine that one of these functions is to guard against infection of the genital tract during pregnancy, labor and the puerperium. The rapid changes that take place following delivery may lead to pathologic consequences. Perhaps additional safeguards can be found to maintain the elaborate set-up already present in a high degree of efficiency, thereby minimizing undesirable sequelae.

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DISCUSSION

DR. GEORGE W. BARTELMEZ.—The relationship between activity in the vaginal epithelium and the concentration of estrogenic hormone seems to be very definite. Yet it is well to remember that the endocrines associated with the female reproductive system represent a very delicately balanced mechanism. The introduction of any hormone involves a change in the organism as a whole. It is possible that estrin does nothing more than increase the circulation in the reproductive tract and as a result we get greater mitotic or secretory activity. On the other hand, it may be that other hormones are also involved. At the present time it looks as if in the absence of the anterior lobe of the hypophysis all the characteristic effects of estrin can be obtained. No one has as yet removed all the other endocrines from an animal and then used estrin.

I should like to ask Dr. Davis whether he has seen any evidence of reduction in the activity of the vaginal epithelium weeks or months before the end of pregnancy. There are not a few instances in which it looks as though the ovary had become quite inactive long before the end of pregnancy. Stieve has described two cases in which he could find no evidence of a corpus luteum in either ovary during the last third of pregnancy. It would be interesting to know whether in such instances there was evidence of regression in the vaginal epithelium, even though plenty of estrin is being produced in the placenta.

DR. ARTHUR KOFF.—The recent work by Meyer and others seems to show that the vagina has a double origin. Certainly most of the upper part of the vagina is derived from the müllerian system, and some portion of the lower third, just how much it is impossible to say, is derived from the urogenital system.

It is important to take biopsies in work such as this from the upper third of the vagina, for that portion which is derived from the urogenital system may not take part in the cyclic changes of the rest of the genital tract.

DR. ROBERT M. GRIER.—I would like to ask Dr. Davis whether there were any special changes noted in those mothers who were nursing babies. Many nursing mothers do not menstruate. It has been assumed they do not ovulate.

If this is true, then there should be no ripening follicles to produce estrin and the vaginal epithelium should show the absence of this hormone in the lack of full development of a squamous layer much as is seen before puberty and after the menopause.

DR. DAVIS (closing).—In a number of our cases we noted a decrease in the thickening of the squamous epithelium and likewise a decrease in glycogen a week or ten days before the onset of labor. That did not occur in all cases. What we presented here was a typical case, one of twenty or twenty-one typical cases. Whether this decrease of the activity of the squamous epithelium is due to decrease in estrogenic hormone we cannot say. We have as yet had too few good curves of estrogenic hormone during pregnancy and after delivery.

All our biopsies were taken in the upper third of the vagina. I agree it is important to take all the biopsies from the part of the vagina that we know definitely is of müllerian origin.

We did not correlate our study with nursing. It is certainly an interesting point to note whether nursing mothers do get changes in the squamous epithelium during the postpartum period. We did attempt to correlate the vaginal changes with the recurrence of the menses to see whether normal cyclical activity occurred before or after the onset of menses.

Bland, Brooke and Rakoff, A. E.: The Incidence of Trichomonads in the Vagina, Mouth and Rectum, J. A. M. A. 108: 2013, 1937.

This study of the incidence of trichomonas from the vagina, mouth, and rectum of 200 women employed wet smears, stained slides and culture methods. Vaginal infestation with trichomonas was common, occurring in 23 per cent of the group. Buccal infestation occurred in 16.5 per cent of the patients, while intestinal trichomonas was comparatively rare, being present only in 1.5 per cent of the women.

It was demonstrated that the wet smear method is the most efficient for the diagnosis of *Trichomonas vaginalis*, while the culture method was more superior for the detection of the intestinal and buccal trichomonads. Women harboring vaginal trichomonas did not show an appreciable higher percentage of buccal or intestinal trichomonads than were noted for the group at large. Only one woman harbored all three organisms.

Rectal contamination was regarded as an improbable source of vaginal infestation in view of the rarity of intestinal trichomonas among women with *Trichomonas vaginitis*. Of three patients harboring intestinal trichomonads, only one was positive for *Trichomonas vaginalis* despite the fact that the flagellates could be regularly demonstrated in the feces over long periods of time. Autoinfestation with buccal trichomonads was also considered an unlikely source of vaginal infestation because the dual incidence of these organisms was not more than would be expected from chance distribution. A comparison of the incidence of trichomonads from the bowel and mouth indicates that intestinal infestation probably does not result from ingestion of the buccal forms.

Unlike the intestinal and buccal trichomonads, *Trichomonas vaginalis* was not cultivable at room temperature and was considered physiologically different.

Approximately 500 clinic and private patients were studied, who had been under observation in the ante-partum clinic or private office and were apparently in good health. We sought to demonstrate the efficiency of either agent by noting the behavior of the uterus and the amount of blood loss during and after the third stage, and subsequently, the rate of involution, the occurrence of abnormal bleeding, and the incidence of foul lochia, all of which were felt to be proper criteria of the response of the uterus to oxytocic action. These observations were always checked by another worker besides myself, in order to eliminate one-man bias.

The standard procedure already in use, and the criteria for employment of its several details, were as follows:

1. At the end of the third stage, one ampoule of "pitocin" and one ampoule of "ernutin," an ergotamine tartrate preparation (Preparation "A" in Table I) were given intramuscularly.
2. If brisk bleeding occurred, or any bleeding continued for more than three minutes, or the uterus did not contract firmly within this period, the same injection was repeated.
3. If this were not effective within a similar time, an intravenous injection of "ergotrate," an ergonovine preparation (Preparation "B" in the table) was given.

These procedures had been found adequate for the control of simple inertia, it being, of course, understood that other causes of bleeding had been ruled out.

In testing the new preparation, the 500 cases observed were divided approximately in half, all patients admitted each day being assigned in alternation to either of the two groups, without other selection. In Group I the above routine was applied as formerly. In Group II the new preparation, "ergoklonin," an ergonovine preparation (Preparation "C" in the table) was substituted in the above routine in place of Preparation "A" and the pitocin. This being the only difference in management between the two groups, it is believed that differences between the two groups in the ratio of delayed to prompt reaction time express the relative difference in efficiency between Preparations "A" and "C." Table I exhibits the alternative management of the two groups.

TABLE I. ALTERNATIVE MANAGEMENT

AT END OF THIRD STAGE	FOLLOWED IF NECESSARY IN 3 MINUTES	FOLLOWED IF NECESSARY IN ANOTHER 3 MINUTES
Group I. 1 ampoule of pitocin plus 1 ampoule ernutin, intramuscularly (Preparation "A")	Repetition of same	1 ampoule ergotrate intravenously (Preparation "B")
Group II. Ergoklonin 20 minims intramuscularly (Preparation "C")	Repetition of same	As above

NOTE: In both groups, if the bleeding during the first three-minute interval were urgent, the injection in Column 2 was omitted, and that in Column 3 was used instead.

3. Traumatized or devitalized tissues were present in all infected cases.

4. Infection or contamination may be considered exogenous in origin being more common after delivery.

5. Treatment with antitoxin and local zinc peroxide was followed by complete recovery in all of the endometritis cases.

The bacteriologic work in the above study was carried out by Emma M. Hill, under the supervision of Dr. Frank L. Meleney, in the Bacteriological Research Laboratory of the Department of Surgery, College of Physicians and Surgeons, Columbia University, New York City.

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OBSERVATIONS ON THE RELATIVE EFFICIENCY OF TWO TYPES OF ERGOT PREPARATIONS IN THE CONTROL OF POST-PARTUM BLEEDING*

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POST-PARTUM bleeding often is an alarming incident of the third stage of labor. We constantly seek to combat it from a preventive as well as from a therapeutic standpoint.

Among the means to this end is the use of oxytocic agents. Of these, those whose active principles are derived from the pituitary are rapid, powerful, but evanescent in action. Those whose active principles are derived from ergot are fairly powerful, less rapid, but more prolonged in action.

Hence, it has been our routine in this clinic to use a combination of a pituitary extract with an ergot derivative, given intramuscularly at the end of the third stage.

Heretofore, the most satisfactory of the numerous ergot preparations available has seemed to us to be one of the products offered by several reputable manufacturers, the active principle of which is the alkaloidal salt, ergotamine tartrate.

But more recently, there have been offered by a number of good houses preparations whose active principle is the newly developed so-called alkaloidal residue of ergot, ergonovine. Desiring to establish whether such products are actually superior in clinical effectiveness to previously available ones, this study was undertaken to test the relative efficiency of one of the newer preparations, "ergoklonin," compared with that of a standard preparation of ergotamine tartrate.

*Read before the Section of Obstetrics and Gynecology, N. Y. Academy of Medicine, May 25, 1937, at a Resident's Program.

was not a ponderable factor in prolonging the reaction time of the uterus. This is shown in Table IV.

TYPE IV. TYPE OF DELIVERY WITH REACTION TIME

	GROUP I					GROUP II				
	NO. OF CASES	NOT OVER 3 MIN.	%	OVER 3 MIN.	%	NO. OF CASES	NOT OVER 3 MIN.	%	OVER 3 MIN.	%
Spontaneous	175	126	72.0	49	28.0	219	165	75.4	54	24.6
Elective low forceps	55	43	78.0	12	22.0	13	8	62.0	5	38.0
Low forceps	15	12	80.0	3	20.0	13	10	76.0	3	24.0
Midforceps	6	4	66.6	2	33.3	3	2	66.6	1	33.3
Breech	8	7	83.3	1	16.6	10	7	70.0	3	30.0
Abortion	1	1	100.0	0	0					
Total	260	193		67		258	192		66	
Percentage		74.2		25.8			74.4		25.6	

This table shows that the type of delivery was not a significant factor in the observed difference in reaction time as between Series I and II exhibited in a previous table.

The influence of several types of anesthesia were then assessed. The results of these observations are shown in Table V.

Table V shows that gas oxygen gives the best results as to incidence of relaxation; ether, even when used only in combination, increasing

TABLE V. TYPE OF ANESTHESIA WITH REACTION TIME OF UTERUS

	GROUP I				GROUP II			
	NOT OVER 3 MIN.	OVER 3 MIN.	TOTAL	% OVER 3 MIN.	NOT OVER 3 MIN.	OVER 3 MIN.	TOTAL	% OVER 3 MIN.
Ether	38	28	66	40.0	70	35	105	33.3
Gas, oxygen, ether	94	24	118	20.0	70	19	89	21.3
Gas and oxygen	42	9	51	17.17	37	7	44	15.9
Spinal	11	4	15	26.6	9	4	13	37.0
CH ₂ Cl	1	1			1	0		
None	6	0			5	1		
Local	1	1			0	0		

the incidence, and when used alone causing the highest incidence of all. But there is no evidence that the influence of anesthesia modifies the conclusions as to the superiority of ergonovine.

Perhaps the most notable difference in oxytocic efficiency of the two agents under consideration was noted in following the two series of cases through their post-partum courses and is exhibited in Table VI.

Doubtful cases, that is, cases in which there was question of retained secundines or in which there was doubt as to the actual amount of bleeding, were discarded. As we have previously seen that there was no significant difference between the two groups in operative incidence, there being an actually higher incidence of low forceps in Group II, the comparison given in Table VI is the more forceful. It

The gross difference between the two groups is shown in Table II.

TABLE II. GROSS DIFFERENCE BETWEEN TWO GROUPS

	TOTAL PATIENTS	PATIENTS NEEDING SECOND DOSE	PATIENTS NEEDING IN- TRAVENOUS INJECTION	PATIENTS NEEDING BOTH	TOTAL NEED- ING ADDITIONAL TREATMENT
Group I	260	24	41	2	67
Group II	258	18	12	4	34

OR

Group I	Initial injection efficient in	74%
Group II	Initial injection efficient in	87%

OR

About twice as many cases in Group I required additional medication as in Group II.

These results would seem to demonstrate the relatively higher efficiency of ergonovine as compared to ergotamine tartrate and pitocin.

But recognizing that the factors influencing the third stage of labor and the puerperium are many, a proper study must necessarily include, besides the efficiency of oxytocics, such matters as type of individual, general physical condition, complicating conditions, age, parity, duration of labor, type of delivery, anesthesia, and the actual management of the third stage in all its details. We have therefore included observations on several of these. The influence of others we believe is fairly averaged between the two groups by the size of the series included in the study.

The general condition of the patient is checked during her antepartum course.

The few abnormalities noted were fairly evenly divided between the two groups as shown in Table III.

TABLE III

Group I		
	Mild toxemia	11
	Rheumatic heart disease	4
	Colloid goiter	1
	Generalized syphilis	1
	Post-partum eclampsia	1
Group II		
	Mild toxemia	7
	Uterine fibroids	1
	Generalized syphilis	3

The type of delivery would roughly indicate the length and severity of labor.

We considered the effect of the type of delivery in each series on the reaction time of the uterus. The several types of delivery in each series were fairly well divided with the exception of the relatively large number of elective low forceps in Group I. It can be concluded that as far as this series of cases is concerned the type of delivery

TRICHOMONAS VAGINALIS VAGINITIS

A COMPARATIVE STUDY OF TREATMENT AND INCIDENCE

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FOR the past thirteen months a routine search has been made for *Trichomonas vaginalis* in all patients visiting the Obstetrical and Gynecological Clinic of the United States Naval Hospital, San Diego, California. This clinic affords accommodation for some 22,000 persons yearly.

During the period from Feb. 3, 1936, to March 3, 1937, a total of 5,712 obstetric and gynecologic patients were examined routinely for the trichomonas. All patients were white females ranging in age from fourteen to fifty-five years, the average age being 26.3 years.

INCIDENCE

The 5,712 examinations yielded 1,405, or 24.6 per cent, smears positive for *Trichomonas vaginalis*. Cultures were not made as such a procedure would have overburdened the laboratory. In only one case was the patient past the menopause. She was fifty-five years of age and entered the clinic for burning of the vagina and adjoining vulva. Three of the patients appeared to be virgins upon examination. It was noted that the organisms were more often found soon after a menstrual period or delivery. Records are not complete enough to give exact figures as to the percentage of smears positive following menses as compared to those before menses, but in the prenatal patients it was found in 20.3 per cent of the patients as compared to 33 per cent of the post-partum cases examined. It, therefore, was found less frequently in the prenatal patients than in the average gynecologic patients. This is not in accord with many reports.

There was one case of ulcerative proctitis in which the *Trichomonas vaginalis* was believed to have been the causative agent. This case is reported in detail further on in the report as no other such case has been noted in the literature.

DIAGNOSIS

A diagnosis was made in the majority of the cases on the saline preparations alone as only 211 or 15 per cent of the cases complained of the symptoms one expects to find. The 15 per cent complained mainly of itching and burning of the vagina and adjoining vulva, associated with a slightly greenish, watery discharge. Other complaints were: leucorrhea, burning on urination, and pain in the left lower quadrant associated with painful coitus. Only when no other pathology could be found to account for the pain was the trichomonad infection credited with causing it. There were 295 or 21 per cent of the patients complaining of these obscure complaints which may or may not have been due to the trichomonad. In 899 or 64 per cent of the cases the patient had no complaint which would lead one to suspect a trichomonad infection.

ASSOCIATED CONDITIONS

As was stated above, 211 or 15 per cent of the patients with *Trichomonas vaginalis* vaginitis presented themselves for symptoms ascribed to that condition. One patient had an associated proctitis credited to trichomonas infection.

TABLE VI. CASES SHOWING LATE POST-PARTUM BLEEDING

		G-O-E	ETHER	G-O	SPINAL	TOTALS
Spontaneous	Group I	7	8	8	1	24
	Group II	0	1	0	0	1
Elective low forceps	Group I	3	1	0	2	6
	Group II	0	0	1	0	1
Low forceps	Group I	1	0	0	1	2
	Group II	0	0	0	0	0
Midforceps	Group I	0	2	0	1	3
	Group II	0	0	0	0	0
Totals	Group I	35				
	Group II	2				

is also evident that ether, which has been shown to increase immediate bleeding, was not a predominant factor in the above table.

A number of cases having foul lochia during the post-partum course were also listed. Of these there were 26 in Group I, 5 of which had a second dose of oxytocic and three of which had intravenous ergotrate. In Group II there were 19 patients, with approximately the same number of patients receiving a second or third dose of medicine. One-half the patients in Group I exhibiting foul lochia also had post-partum bleeding. Accurate conclusions cannot be drawn from the relatively small number of observations made of this symptom. The actual results would indicate a higher incidence in Group I. It is also evident that this symptom occurs relatively more frequently in patients who have had excessive bleeding during the third stage or subsequently.

No appreciable difference was found in the number of hospital days as between the two groups.

SUMMARY

Approximately 500 unselected patients were observed during the third stage of delivery, the immediate post-partum period and the subsequent puerperium, with reference to the amount of immediate and secondary bleeding, uterine tone, and the appearance of foul lochia.

These patients were divided into two groups, one of which was treated with pitocin and ergotamine tartrate, and the second of which was treated with an ergonovine preparation.

Comparison between the two groups would appear to establish:

1. That the ergonovine preparation used was more efficient in preventing and controlling abnormal bleeding than the ergotamine tartrate preparation. This difference is accentuated by the fact that the ergotamine tartrate was used in combination with a potent pituitary extract.

2. That ether anesthesia predisposes most to post-partum bleeding and nitrous oxide least, of the small group of anesthetic agents studied.

3. That the type of delivery had no essential effect on the incidence of post-partum bleeding.

4. That the occurrence of abnormal post-partum bleeding appears to predispose to sapremic infection of the uterus.

5. That none of the corollary factors concerned in this study modifies the first conclusion as to the clinical superiority of ergonovine preparations over older forms of ergot derivatives.

METHODS OF TREATMENT AND RESULTS WITH EACH METHOD

Carbarsone.—Early in the series all patients were treated with P-carbamino phenyl arsenic acid.* During the first week the patient used 5 gr. of carbarsone and 5 gr. of sodium bicarbonate dissolved in half an ounce of warm water and instilled into the vagina upon retiring. The following morning a 2 gr. carbarsone suppository was inserted into the vagina. On the morning of the seventh day a sodium bicarbonate douche was taken and the patient reported for the taking of smears. If smears were positive the same routine was continued for another week. When the smears became negative only a 2 gr. suppository was used in the vagina at bedtime. This was continued until the patient had been under treatment for a period of forty-two days. Smears were taken following each of three menstrual periods before the patient was discharged.

Treatment by this method was given to 210 patients or 14.94 per cent of the total series. Three patients or 1.43 per cent had received previous treatment; 154 or 73.33 per cent were cured with one course; 53 or 25.24 per cent required two courses before being cured. Three patients or 1.43 per cent were not cured after two courses, and were considered failures by this method. No reactions were encountered in this group of patients.

Vioform.†—The second medication used in the treatment was iodochloroxy-quinoline. This is a very light weight powder. The vioform powder was mixed with glycerin to form a thin paste. The best proportion of the mixture being 15 gm. of vioform to 22 c.c. of glycerin. This paste was applied to the vagina with applicators while rotating a bivalve speculum in the vagina. This paste was applied daily for a week and smears were then taken. If positive, the same treatment was continued for another week. When smears became negative, the paste was applied on alternate days and the patient was instructed to take two douches of 0.5 per cent lactic acid daily on the other days until treatment had been kept up for a period of forty-two days. Rechecks were made after each of three menstrual periods before the patient was discharged.

This method of treatment was given to 500 or 35.59 per cent of the total series. Seven patients or 1.4 per cent had received treatment previously; 381 patients or 76.2 per cent were cured with one course; 118 or 23.6 per cent required two courses before remaining negative. One case or 0.2 per cent was positive after two courses and was considered a failure by this method. No reactions were noted in this group.

Silver Picrate.—The silver picrate method of treatment proved quite simple, effective, and time saving. It was, therefore, used on more patients than any other single method. This method consisted in washing the vagina with tincture of green soap and water, drying, and insufflating the silver picrate-kaolin powder‡ into the vagina, in the proportion of one part of silver picrate to ninety-nine of kaolin. This was done once each week and each intervening night the patient inserted a suppository of 2 gr. of silver picrate* in a boroglyceride-gelatin base. Smears were taken each week and treatment continued for a period of forty-two days. Smears were taken following each of three menstrual periods. Two patients in this series developed a rather severe dermatitis of the vulva and buttocks, but the condition cleared rapidly when the treatment was completed. Neither case necessitated interruption of the treatment. This treatment causes marked staining of the skin about vagina and rectum, but decolorizes rather rapidly when the course is completed.

This method was used in 695 or 49.47 per cent of the entire series. Eleven or 1.73 per cent had been treated by other methods; 554 or 79.71 per cent were cured with one course; 141 or 20.29 per cent required two courses. There have been no failures noted in this group.

*Manufactured under the trade name Carbarsone by Eli Lilly and Company.

†Manufactured by the Ciba Co.

‡Suppositories and powder manufactured by John Wyeth & Brother, Inc.

In 899 or 64 per cent of the cases the organism was found only because of routine examination as the patients were examined for fibroids, irregular menses, amenorrhea, suspected pregnancy, etc. Three virgins or 0.21 per cent had a profuse, clear, watery discharge but did not complain of itching. These were associated with the Döderlein bacillus infection, and it is believed that this type of discharge was due to a pathogenic abundance of these bacilli. Some 175 or 12.455 per cent had a gonorrheal endocervicitis, while 116 or 8.26 per cent had a mixed infection of the endocervix. One patient had an associated monilia infection.

TRICHOMONAS VAGINALIS PROCTITIS

D. M., a white female beauty parlor operator, aged 27 years, presented herself at the clinic Dec. 3, 1936 complaining of a profuse greenish, watery discharge associated with marked itching and burning at the entrance of the vagina. She had never been pregnant, and menses were $14 \times 28 \times 6$. The condition began ten days following her last menses. She denied any venereal infection. History was otherwise irrelevant.

Pelvic examination revealed a marital introitus with firm perineum. Bartholinian glands and Skene's ducts appeared normal. The cervix was nulliparous in type. The vagina was moderately red and was excoriated at its entrance. There was approximately 10 c.c. of greenish watery material in the vagina. Smears of this were taken for the *Trichomonas vaginalis*. Cervical and urethral smears were made for Neisserian organisms. The uterus was normal in size and position. Both adnexa were normal.

The saline preparation was loaded with trichomonas. The other smears were negative for Neisserian organisms. The treatment consisted of silver picrate powder insufflations once weekly and suppositories each night for six nights. The vagina was scrubbed well with tincture of green soap and water, then dried before the powder was insufflated. After one week, the patient was symptom free and smears were negative. At the end of the second week the smears were positive in spite of continued treatment. At the end of the third week smears were again negative and remained so until the fifth week when positive smears were again obtained. At the end of six weeks smears were negative and the patient was still symptom-free.

Treatment was discontinued Jan. 14, 1937, and the patient was told to return ten days later for an examination.

When the patient returned all symptoms had recurred and, in addition, she was complaining of burning of the rectum and painful defecation. A proctoscopic examination showed the rectum and lower sigmoid to be very red throughout, and many dirty, gray flecks of exudate, pinhead in size, completely covered the mucosa of the rectum and lower sigmoid. When this material was scraped away a small ulcer extending about half the depth of the mucosa was revealed. There was slight oozing from each of these areas. There was no tendency for the ulcers to coalesce. The smears taken from the base of these ulcerations showed many motile trichomonas morphologically identical with those in smears from the vagina taken at the same time. No other pathogenic organisms were found.

The same treatment was begun again for the vaginal infection and one insufflation given into the rectum which relieved pain and itching but resulted in a severe diarrhea. Following this only the silver picrate suppositories were used in the rectum. Two weeks of treatment resulted in negative smears from vagina and rectum associated with complete healing of the lesions in the rectum and sigmoid.

A check on this patient six weeks after discharge from the clinic revealed that she had been entirely free of symptoms, and smears were still negative from both rectum and vagina. A recent check, approximately three months after discharge, shows no organisms or symptoms present. The patient says she is in excellent health.

believed that such cases would more probably be due to reinfection. Unfortunately, the husbands of these women could not be examined; so no attempt was made to determine the source of infection for statistical purposes.

The case of proctitis is reported to call attention to a condition which may be occurring as a clinical entity more often than is recognized. Due to the fact that the organisms are thought to occur as nonpathogenic inhabitants of the intestinal tract, most people have thought it incapable of causing lesions of clinical significance in this location. Perhaps, some of the cases with left lower quadrant pain were due to a sigmoiditis and proctatitis caused by the trichomonad but were not recognized as no search was made for it in the intestinal tract. It would be interesting if those studying the stools routinely would also examine the rectum and sigmoid for manifestations of sigmoiditis or proctitis. However, it may be that the pain in the lower quadrant of these patients is due to *Trichomonas vaginalis* infection of the tubes, ovaries, or peritoneal cavity as suggested by Hees.

TABLE I. RESULTS OF TREATMENT

METHOD USED	CASES	%	HAD R BEFORE		CURED 1ST R		CURED 2ND R		FAILURES	
			CASES	%	CASES	%	CASES	%	CASES	%
Carbarsone	210	14.94	3	1.43	154	73.33	53	25.24	3	1.43
Vioform	500	35.59	7	1.4	381	76.2	118	23.6	1	0.2
Silver Pierate	695	49.47	11	1.73	554	79.71	141	20.29	0	--

Weinstein, Bogin, Howard and Finkelstone¹ and others state that they have never found Döderlein bacilli with trichomonas infection, but in the cases herein reported the bacilli were in very great amounts and were identified by cultures and smears. Apparently the trichomonas organism in these cases had become accustomed to the acid flora caused by the Döderlein bacilli; or else the infection by the trichomonas had been too recent for the bacilli to disappear. Both organisms were absent after two weeks and remained so for the remainder of the treatment and at the time of the three-month re-examination.

SUMMARY

1. The incidence of *Trichomonas vaginalis* infection among 5,712 obstetric and gynecologic patients of the Obstetrical and Gynecological Clinic at the U. S. Naval Hospital, San Diego, California, was found to be 24.6 per cent for all patients examined or 3.69 per cent when only those with typical symptoms were considered.

2. In post-partum cases the incidence was 33 per cent, as compared to 20.3 per cent in the ante-partum cases.

3. *Trichomonas vaginalis* vaginitis as a recognized clinical entity occurred in only 15 per cent of the cases.

4. Some patients had left lower quadrant pain and painful coitus with no other findings to account for it.

DISCUSSION

From a review of the literature one finds three striking facts: (1) There is no general agreement regarding the pathogenesis of this organism; (2) the source of infection is far from being agreed upon; and, (3) the methods of treatment are extremely varied.

This report is being made for a threefold purpose: (1) To present the figures of occurrence of true pathogenic cases, and of incidental cases; (2) to give a simple, effective, and time-saving means of treatment; and, (3) to report a case of *Trichomonas vaginalis* proctitis occurring as a clinical entity.

Since only 15 per cent of the cases of *Trichomonas vaginalis* vaginitis had clinical symptoms it is very probable that only those cases would have been recognized had not routine preparations been examined. Therefore the corrected figure for this series would be 211 cases in a total of 5,712 or 3.69 per cent of the entire series of cases which had clinical symptoms definitely suggestive of *Trichomonas vaginalis* vaginitis.

From the above figures, one who believes the trichomonas a markedly pathogenic organism would certainly be surprised at the relatively small percentage of the patients (15 per cent) giving clinical symptoms sufficient to cause them to seek medical aid for that reason alone. On the other hand, that 15 per cent or 211 patients were cured of all complaints when adequately treated. Thus, certainly, this organism is capable of producing a severe, and disabling vaginitis. However, the author is led to believe that the pathogenicity of the trichomonad is generally exaggerated. Again, why are some cases of the infection so severe and others symptomless? Could it be that the organisms occur in a smooth and a rough or pathogenic and nonpathogenic form? These are questions that must be answered before adequate progress can be made in treating and controlling these cases.

When the three methods of treatment employed are reviewed, it is seen that the results very closely parallel each other, though figures indicate a slight advantage in the use of the silver picrate method (Table 1). The main advantage this method offers over the others is the ease with which it can be used as compared to the other two, and this probably accounts for the difference in the results; for it is generally conceded that the more difficult methods are less often applied correctly, especially by the patients themselves. It is believed that the possibility of reactions following the use of carbarsone is not a factor sufficient to cause abandoning this method. The vioform is very effective, but too time consuming for a large clinic. All patients in this clinic were treated for a period of six weeks in order that treatment would cover at least one menstrual period, unless the patient was pregnant. It is felt that this is a very important factor in the treatment of this infection, and that it will prevent many recurrences. Attention is called also to the fact that treatment should continue during the menstrual period. In the more recent cases of this series the patients have only been followed for a period of three months and so may show subsequent return of the infection, but it is

IDENTIFICATION OF YEASTLIKE ORGANISMS ISOLATED FROM THE VAGINAL TRACTS OF PREGNANT AND NONPREGNANT WOMEN

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YEASTLIKE organisms have been cultured frequently from the external genitalia and vaginal tracts of women suffering from vulvovaginitis. Proof of the etiologic relationship of these fungi to mycotic vulvovaginitis is complicated by the fact that yeasts also occur in a significant percentage of women who show no signs or symptoms of vulval or vaginal irritation. Attempts to correlate the presence of these fungi with the clinical findings are handicapped by the lack of practical methods for identifying yeastlike organisms.

Castellani's¹ classification which is based on the ability of the organism to ferment certain carbohydrates has not been found practical. Benham² accomplished much in the way of correlating the morphologic, biologic and serologic characteristics of the yeastlike fungi but her methods of identification are too complicated for routine use. The identification key proposed by Stovall and Bubolz³ is much simpler in technique but others^{4, 5} have found strains which cannot be classified in one of the three types proposed by these authors.

Our study describes the methods developed for the identification of 68 strains of yeastlike fungi isolated from the vaginal tracts of pregnant and nonpregnant women. These fungi were isolated during a routine study of the complete vaginal flora by Carter and Jones,⁶ and no correlation with the clinical findings was attempted. Representative strains were obtained from Drs. Benham and Stovall, and a comparison of our technique with the methods described by these authors was thus possible. We present only the details of the procedures necessary for identification. A review of the literature with a more complete discussion of terminology and methods of classification is to be published elsewhere.

MATERIALS AND METHODS

Sixty-eight strains of yeastlike fungi were isolated from the vaginas of 52 pregnant and 16 nonpregnant women. In a nonpregnant patient a sterile speculum was inserted and the swab smeared over the posterior fornices of the vagina. Care was taken not to touch the speculum with the swab. In a pregnant woman no speculum was used; the labia were spread by an assistant and the swab was inserted directly into the vagina. All swabs were streaked on Sabouraud's slants and were smeared

5. Routine examination accounted for 64 per cent of the cases being found; 15 per cent were recognized clinical entities; 0.21 per cent occurred with a pathogenic abundance of Döderlein bacilli; 12.455 per cent were associated with gonorrheal endocervicitis; 8.26 per cent had a nonspecific endocervicitis; and 0.075 per cent occurred with monilia infection.

6. A case of *Trichomonas vaginalis* proctitis is reported.

7. Comparative results of treatment with carbarsone, vioform, and silver picrate are given.

8. Some pertinent facts from the literature are cited.

The author wishes to express his most sincere appreciations to Dr. John E. Porter, Senior Obstetrician and Gynecologist, at this Clinic for referring his cases to the author for study and treatment.

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SEROLOGIC STUDY OF HEMOLYTIC STREPTOCOCCI FROM THE THROAT, NOSE, AND VAGINA OF ANTE- PARTUM OBSTETRIC PATIENTS

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CONVINCING evidence is accumulating that the hemolytic streptococci encountered in puerperal infections are derived almost entirely from extragenital sources. Since Lancefield¹ separated these organisms into definite groups on the basis of precipitin reactions, there has become available a useful, though somewhat laborious, method for determining whether or not a given strain is pathogenic for human beings. This author has shown that practically all strains derived from human infections can be grouped into a single class, Group A. The human body may harbor organisms of the other groups, notably B, C, D, F and G, which are ordinarily not pathogenic, although isolated cases suggest that occasionally they may give rise to human infection.

Lancefield and Hare² classified many strains of hemolytic streptococci from the vaginas of three series of obstetric patients in Queen Charlotte's Hospital, London, using the precipitin technique. The first series included 46 strains obtained from clinically typical cases of puerperal infection; all but one belonged in Group A. The remaining strain was a Group G organism associated with a *Staphylococcus aureus* septicemia. The second series comprised 85 strains isolated from 837 post-partum women who were either afebrile or who had had only slight increases in temperature during the puerperium. There was only one Group A organism and that was obtained from a patient who had an afebrile convalescence. The authors gave consideration to the possibility that some strains of other than Group A might have been responsible for certain of the 18 mild infections, but reached no conclusions. The

third series consisted of 13 strains isolated from 855 ante-partum women. Only one patient had a slight pyrexia during the puerperium. None of the 12 strains tested was in Group A. One strain was lost.

Leonard Colebrook³ has presented an excellent summary of the sources of hemolytic streptococci involved in puerperal sepsis and has stressed the importance of the respiratory tract as a reservoir for Group A organisms. The recently infected respiratory tract is considered of greatest significance, while open septic conditions, healthy carriers, and the possibility of air borne infections are given secondary consideration. The rigid investigation of the sources of puerperal fever carried out by Dora Colebrook⁴ likewise incriminates the respiratory tract of either the mother, some member of the family, or one of the attendants in a large percentage of cases.

In view of these findings it was decided to determine the incidence of significant (Group A) streptococci among the patients on the obstetric wards of the University Hospital. Accordingly bacteriologic examinations of the respiratory and vaginal tracts of five hundred women have been made.

METHODS

Each patient was examined shortly after her entry into the hospital, usually within twenty-four hours. Throat cultures were taken by depressing the tongue and rubbing the tonsillar region thoroughly with a sterile swab. Nose cultures were taken on the last 300 women of the series by rotating a sterile swab inserted into the nostrils. Vaginal cultures were taken before digital examination. The labia were separated and a sterile swab inserted deeply and rotated. Throat cultures were repeated five days later.

All swabs were immediately inoculated onto blood agar plates. Throat and nose cultures were incubated aerobically and vaginal cultures both aerobically and anaerobically. All plates were examined at the end of twenty-four and forty-eight hours for hemolytic streptococcus colonies.

In classifying the isolated organisms the "tentative methods for isolation and identification of hemolytic streptococci" as outlined by Coffey⁵ were followed.

The precipitin technique was carried out as follows: Antisera were obtained by immunizing rabbits with dead organisms representative of the various groups, as furnished by Lancefield.⁶ Each antiserum was tested against acid extracts of the homologous organism and of one other known member of the group, by layering 0.1 c.c. of the extract over an equal volume of serum in a small tube. The formation of a ring of precipitate at the junction of the two liquids indicates a positive reaction. All isolated streptococci were classified according to their reactions with the prepared antisera. No cross reactions were encountered.

TABLE I. SOURCE OF 53 STRAINS OF HEMOLYTIC STREPTOCOCCI ISOLATED FROM 500 OBSTETRIC PATIENTS

SOURCE; NO. OF PATIENTS	NO. OF STRAINS	PERCENTAGE
Throat (500 patients)		
First culture only	23	4.6
Second culture only	15	3.0
First and second cultures	6	1.2
Nose (300 patients)		
One culture only	6	2.0
Vagina (500 patients)		
One culture only	3	0.6

*We are glad to acknowledge this fine cooperation, which has in large part made possible the conclusion of this study. Our thanks are also extended to Dr. R. Hare, Toronto, who kindly furnished a Group K organism.

RESULTS

A total of 53 strains of streptococci producing soluble hemolysins were isolated from the 500 women. The sources of these strains are indicated in Table I.

Serologic study of the organisms permitted all strains to be placed in 4 of the 9 recognized groups. Table II lists the groups and sources.

TABLE II. SEROLOGIC GROUPING (LANCIEFIELD) OF 53 STRAINS OF HEMOLYTIC STREPTOCOCCI ISOLATED FROM 500 OBSTETRIC PATIENTS

GROUP (LANCIEFIELD)	SOURCE	NUMBER	PERCENTAGE OF TOTAL
Group A	Throat	33	62.3
	Nose	3	5.7
Group B	Vagina	2	3.8
Group C	Throat	3	5.7
	Nose	2	3.8
	Vagina	1	1.9
Group G	Throat	8	15.1
	Nose	1	1.9
	Total	53	100.2

COMMENT

There were 44 positive throat cultures in five hundred ante partum obstetric cases, but in only six individuals were hemolytic streptococci found at both examinations (on admission and five days later).

The observation that 23 patients had positive throat cultures on the first examination and negative cultures five days later may be explained by the fact that many of these women were brought to the hospital in ambulances, often from some distance. Cold weather in addition to fatigue undoubtedly encourages mild throat infections. A number of these patients complained of having "scratchy" throats at the time of the first examination. A surprisingly small percentage admitted recent sore throat, infected cuts, scarlet fever, or other infections, either in themselves or in members of their families. The conditions under which they lived while in the hospital apparently favored rapid control of throat infections.

Fifteen patients who had negative cultures at the time of entry had positive cultures five days later. This suggests that the latter group acquired the organisms during the five-day period, but the possibility that every throat swabbing was not efficient must be kept in mind. It is well known that the isolation of hemolytic streptococci from the throat is dependent upon such variables as the thorough application of the swab, the recency of active infection, and the possibility that the patient has recently gargled with an antiseptic solution, as discussed in some detail by Colebrook.⁴

Nose cultures were positive six times in the 300 cases studied. In only one instance did the throat also contain hemolytic streptococci.

In keeping with other published data, especially those of Lancefield and Hare,² the strains isolated ante partum from the vagina were not of Group A. Two of the three patients remained afebrile, while the third had a temperature of 100.4° F. on the third day post partum and of 101.0° on the ninth day.

The seasonal incidence of hemolytic streptococci is well brought out by this study which was started on Oct. 19, 1936. One strain was isolated in the remaining twelve days of October, 3 were found in November, 10 in December, 18 in January, 15 in February, and 5 in the first ten days of March, 1937, at which time the series was concluded.

Our data support Coffey's⁶ contention that the precipitin reactions are more reliable than the biochemical tests. All but one of the 53 tested strains fermented trehalose. The exceptional organism, serologically in Group C, alone fermented sorbitol. Two Group B strains from the vagina hydrolyzed sodium hippurate. The final hydrogen ion values invariably were within the limits indicated in Coffey's latest report and need not be elaborated.

Table III presents the puerperal morbidity in the 500 women and groups the streptococci isolated ante partum. No post-partum cultures were made.

TABLE III. ANALYSIS OF PUERPERAL MORBIDITY IN 500 OBSTETRIC PATIENTS, WITH SEROLOGIC GROUPING OF HEMOLYTIC STREPTOCOCCI ISOLATED ANTE PARTUM

	NO. OF PA- TIENTS	PUERPERIUM						GROUP (LANCEFIELD) OF STREPTOCOCCI ISO- LATED ANTE PARTUM FROM WOMEN WITH FEBRILE PUERPERIUM					
		NON- FEBRILE		FEBRILE									
				PUER- PERAL IN- FECTION		INTER- CURRENT IN- FECTION							
				NO.	%	NO.	%	NO.	%				
No Streptococci found	448	361	80.6	77	17.2	10	2.2	SEROLOGIC GROUP					
Streptococci found	52	38	73.1	12	23.1	2	3.8	A		C		G	
								NO.	%	NO.	%	NO.	%
								6	100				
								4	80			1	20
								1	100				
												1	100
First throat cul- ture	23	17	73.9	5	21.7	1	4.4						
Second throat culture	15	10	66.7	4	26.7	1	6.6	4	80			1	20
Both cultures	6	5	83.3	1	16.7			1	100				
Nose culture	5	4	80.0	1	20.0							1	100
Nose and throat	1	1	100.0										
Vaginal culture	3	2	66.7	1	33.3					1	100		

The percentage of puerperal morbidity in the 52 women from whom hemolytic streptococci were isolated ante partum is slightly higher than in the group culturally free from the organisms. It is significant that 11 of the 14 strains isolated ante partum from women who developed fever after delivery were in Group A, one was in Group C, and two were in Group G. On the other hand, 39 strains were isolated ante partum from women who had afebrile convalescences. Of these, 25 were in Group A, 2 in Group B, 5 in Group C, and 7 in Group G. These data suggest that those women who harbor hemolytic streptococci constitute almost as much of a menace to the health of their fellow patients as to their own.

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RESULTS OF TREATMENT IN THE ANTE-PARTUM SYPHILIS CLINIC AT BELLEVUE HOSPITAL*

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THE transmission of syphilis from mother to child can be prevented by early and adequate treatment given to the mother during her prenatal period. In order to do this efficiently, as well as to undertake the study of several other interesting phases of this work, a special clinic, "The Prenatal Syphilis Clinic," was organized at Bellevue Hospital with the cooperation of the Department of Dermatology about three years ago. Upon certain indications, the patients are referred from the regular prenatal clinic. These indications are:

1. A history of a previous definite or suspicious syphilitic lesion.
2. A substantiated history of previous intravenous and intramuscular therapy.
3. A history of repeated premature deliveries, especially if macerated or stillborn, as well as full-term deliveries yielding syphilitic children.
4. All Wassermann reactions other than negative.
5. Suspicious or definite syphilitic lesions in patients attending the prenatal clinic.
6. A suspicious or definite history of a syphilitic infection in the marital partner.

In the Prenatal Syphilis Clinic special history forms are employed and every patient is examined with particular alertness for evidences of her syphilitic infection. Dark-field studies are made on all suspicious lesions. At present patients are also subjected to x-ray study of the heart and aorta. Both a Wassermann and a Kline test are repeated upon the patient, and she is advised of the necessity of having similar tests performed upon her husband and children.

As a result of these examinations, patients are then divided into three categories. First, a group in whom a definite diagnosis of syphilis can be established; these receive treatment immediately. Second, a group who have given suspicious data but upon further checking are found to be free from a syphilitic infection; these are referred back to the regular prenatal clinic. Third, a group who present nothing but repeated mildly positive serodiagnostic reactions; these patients and their babies are subsequently studied to ascertain the significance of such indecisive serodiagnostic reactions occurring in pregnant women.

A study of the last 11,983 deliveries at Bellevue Hospital yielded 489 patients who were diagnosed as syphilitic, an incidence of 4.08 per cent. The present study, however, includes only 325 cases, 295 with acquired syphilis and 30 with definite or probable congenital syphilis. It is the acquired group which is the subject of discussion in this paper.

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The highest attack rate for syphilis occurs during the sixteenth to thirtieth years, which period coincides with the early and most active childbearing period. Belding's¹ impression of the increased frequency of syphilis in multiparas has been borne out in the present study. Of the 295 acquired cases there were 188 multiparas and 107 primiparas, a ratio of $3\frac{1}{2}$ to 2. It is interesting to note that in the 30 congenital cases the ratio was reversed; there were 19 primiparas and 11 multiparas. When the cases were more accurately divided into primigravidas and multigravidas, the preponderance of the latter group was even more emphatically demonstrated, while the congenital group showed a more even distribution as would naturally be expected.

Certain features in the diagnosis of syphilis in the pregnant woman may well be mentioned here. The routine serodiagnostic test is of extreme importance in detecting syphilis in the prenatal period, for there were 254 patients or 86.1 per cent of the acquired group who presented no demonstrable physical evidences of their infection. They were clinically latent in contrast to 41 or 13.9 per cent in whom evidences could be demonstrated. In 33 or 11.2 per cent of the total, early manifestations such as a primary lesion or secondary skin lesions with or without condylomata lata were found. In 8 or 2.7 per cent of the total, late lesions of the cardiovascular or central nervous system were demonstrated.

METHOD OF TREATMENT

The aim in the treatment is primarily to prevent the transmission of the disease to the offspring. The greatest reliance is to be placed upon the use of an arsenical, preferably arsphenamine; along with this a heavy metal, preferably bismuth, is used. Prior to the onset of treatment, a complete physical examination, blood pressure, and urinalysis must be done.

The routine employed varies with: (1) The stage of the syphilitic infection, and (2) the period of gestation.

Treatment is interrupted in the presence of toxemia and other medical contraindications. Severe reactions likewise call for the prompt interruption of arsenical therapy.

Should the patient with early syphilis be seen for the first time during pregnancy, she is treated in much the same fashion as the nonpregnant early syphilitic patient. The treatment of the pregnant woman with latent syphilis varies with the length of gestation. Regardless of the length of gestation, however, treatment is always continuous and uninterrupted by rest periods. When therapy is started during the first trimester, it is well to begin with bismuth as a preliminary to the use of arsphenamine. Alternate series of 4 to 6 intramuscular injections of bismuth and 8 to 10 intravenous injections of arsphenamine are given and treatment is so arranged that the last month or six weeks is to be occupied with the administration of the arsenical. When treatment is started during the second trimester of pregnancy, the method used is continuous alternate therapy with slight overlapping of courses. Before the first course of bismuth is completed arsphenamine is begun, and for the week or two of overlapping the patient appears at the clinic twice weekly. As in the previous group, the arsenical is employed during the last few weeks of pregnancy. In the final group, those who present themselves during the last trimester, continuous combined therapy is used. The arsenical is employed weekly until the end of pregnancy, thus perhaps allowing up to 14 or 15 doses. The bismuth is given on a separate clinic visit each week and may be interrupted for a few weeks fol-

lowing the series of 4 to 6 injections. The major difference between the treatment of the nonpregnant and the pregnant latent syphilitic woman is that in the latter the arsenical receives greater emphasis and the treatment must be continuous. When arsphenamine is employed, the initial dose is 0.1 gm.; this is increased to 0.15 gm. and subsequently to 0.2 gm. at which level it is usually maintained throughout. Occasionally in large women, the dose may be increased to 0.3 gm. If neoarsphenamine is employed, the initial dose is 0.15 gm.; this is increased to 0.2 gm. and finally to 0.3 gm. Occasionally we employed 0.45 gm.

The occurrence and significance of reactions to the arsenical will be discussed later, but it should be said that whenever this drug is employed, one must be ever alert to the possibility of reactions. Urinalyses and blood pressure readings are done prior to each injection and the patient is questioned as to her subjective symptoms following the last dose of the arsenical. Last, the sclerae, mouth, wrists, and elbow bends should be carefully inspected for evidences of toxicity.

RESULTS OF TREATMENT

The relationship of position and presentation in the treated and untreated cases and the operative incidence in the same groups has been studied. The incidence of prematurity in untreated cases was 52.3 per cent. This high incidence was reduced to half in those patients who received treatment prior to the onset of pregnancy. It was further reduced to less than one-fourth, namely 12.9 per cent, in those who received treatment both before and during their pregnancy.

In the untreated group the incidence of vertex presentations was very much lower than normal with a corresponding increase in breech presentations to 13.8 per cent, almost three times the normal. Unquestionably, the reason for the higher incidence of breech presentation is the greater frequency of prematures in this group. With treatment, as the incidence of prematurity diminishes, there is a decrease in breech presentations and a corresponding increase in vertex presentations.

The operative incidence as here noted includes breech deliveries and deliveries by forceps, version, and cesarean section. In the untreated group, operative deliveries accounted for 30.8 per cent of the total while spontaneous deliveries comprised 69.2 per cent. This high operative incidence may be explained by the relative increase in the breech deliveries in this group. In the treated cases, with the resulting increase in full-term deliveries and the associated decrease in breech presentations, the operative incidence was found to be about normal or slightly below, the indications for operative delivery being purely obstetric in nature.

In considering the occurrence of morbidity in patients with and without syphilitic lesions, and how morbidity is influenced by treatment, 10 patients were found with early lesions, mostly genital, who received no treatment; of these 6 or 60 per cent ran a morbid post-partum course. Twenty-four patients with lesions occurring during pregnancy were treated. Many of these patients went into labor after having received a comparatively small amount of treatment, in many instances inadequate to cause a complete subsidence of their manifestations. However, treatment influenced this group so as to bring the incidence of morbidity down to 41.7 per cent from the 60 per cent noted above. In those without lesions who received no treatment or treatment only before or only during pregnancy, the incidence of morbidity was approximately 14 per cent. In those patients without lesions who received treatment both before and during pregnancy, this incidence was diminished to 12.5 per cent, which is still slightly higher than the average of 11.2 per cent. The standard used to determine morbidity is: two or more rises to 100.4° F. or higher, these rises being at least twenty-four hours apart and occurring after the first day post partum.

Patients with syphilis do not show any increase in the incidence of hemorrhage; on the contrary, the incidence is well below normal. This is found to hold true regardless of whether or not treatment was given.

RESULTS OF PREGNANCY IN SYPHILITIC PATIENTS
TREATED AND UNTREATED

One appreciates the ravages of this disease in the prenatal patient by observing the high incidence of prematurity, stillbirths, and neonatal mortality, as well as the incidence of syphilis occurring in those children who are discharged alive. The incidence of maceration observed in the various groups was as follows: 29.2 per cent where no treatment was given, 12.2 per cent where treatment was given prior to pregnancy only, 3.4 per cent where treatment was given during pregnancy only, and 2 per cent where treatment was given both before and during pregnancy. Neonatal deaths due to syphilis occurred in 24.6 per cent of the patients who received no treatment. With treatment this was markedly reduced.

The total early death rate, due to syphilis, of offspring in untreated patients was 62.3 per cent. In the group with treatment only prior to pregnancy, this figure was reduced to 12.2 per cent, and finally to 3.9 per cent in those who received treatment both before and during pregnancy. Poor results are naturally to be expected in the untreated cases even when the babies are discharged alive, for 24.6 per cent of the total babies were found to be syphilitic. In the group who received treatment only prior to pregnancy, the incidence of syphilitic live children was reduced to 4.9 per cent; this is in all probability due to both the treatment given and to the lapse of time which allowed the syphilitic infection to become latent. A higher incidence of syphilitic live children, namely 18.2 per cent, was encountered where treatment was given during pregnancy only; this may be explained by the fact that the infection was more recent and that many of these patients had therapy inadequate to prevent the transmission of the disease. Naturally the best results are to be obtained where treatment was given both before and during pregnancy, there being only 2 per cent of the offspring with syphilis in this group. The status of living offspring is determined by the following routine: The placentas are weighed and then examined grossly and microscopically. Serologic tests are done on the cord blood. In those cases where no treatment was given the mother, a dark-field examination is made on scrapings of the umbilical vein. On the seventh day of life, another Wassermann and another Kline test are done, and the long bones are subjected to x-ray study. After discharge from the hospital, the baby is followed in the pediatric clinic where he is examined and where a Wassermann test is repeated at the end of the first month. If the child is found to be free from disease, the same procedure is employed at the end of three months, and in addition spinal fluid and x-ray studies may be done. Return visits are made at three-month intervals until the end of the first year, and then at six-month intervals thereafter, unless suspicious findings necessitate more frequent visits. One should start treatment only after a definite diagnosis has been established. The babies in this present series have been followed in such a fashion for a period of one month to three years. As the clinic grows older, this period of observation will be prolonged.

A tabulation was made of the results in those patients who received less than 15 injections of the arsenical as compared with those who re-

ceived more than 15 injections. These are further subdivided by consideration of whether or not treatment was given prior to pregnancy. Those who received no treatment prior to pregnancy went to term with almost the same frequency as those who received treatment prior to as well as during pregnancy. It can therefore be concluded that the most essential factor in producing term deliveries is the treatment given the patient during her prenatal period. All those patients who received more than 15 doses of the arsenical without previous treatment went to term; since this group is only 7 in number no significant conclusions can be drawn.

The incidence of macerated stillbirths decreased with increasing amounts of treatment during pregnancy. The total infant death rate due to syphilis in those mothers who received less than 15 arsenical injections was not influenced by the presence of previous treatment. There were no fetal deaths due to syphilis in patients who received more than 15 injections irrespective of previous treatment. This indicates that with 15 or more injections of the arsenical given during pregnancy death due to syphilis can usually be avoided. In those patients who received inadequate treatment during pregnancy, previous treatment increased the incidence of live babies without syphilis from 63 per cent to 80.5 per cent. No conclusions can be drawn from the small group who received at least 15 injections of the arsenical without previous treatment. However, where previous treatment was given as well as more than 15 injections of the arsenical during pregnancy, the incidence of live babies without syphilis rose to 94.7 per cent. This shows that patients who receive treatment prior to as well as sufficient treatment during pregnancy, will produce healthy babies just as often as nonsyphilitic mothers. None of the babies discharged alive developed evidences of syphilis where more than 15 injections were given during pregnancy. To summarize the observations that can be made from this chart, it can be said, that treatment given during pregnancy regardless of previous treatment helped to carry the patient to term; more than 15 injections of the arsenical prevented the transmission of syphilis to the offspring.

Another factor influencing the results of treatment is the period in pregnancy when treatment is begun. While the prevalent impression is that the transmission of the disease from mother to offspring occurs sometime after the sixteenth week, McCord² has recently demonstrated the presence of the spirochete in 9 fetuses under 300 gm. in weight. Therefore, treatment should be begun as early as possible in pregnancy, because the disease may be transmitted during the first few months of gestation.

Treatment during pregnancy helps considerably to carry the patient to term. However, the incidence of term deliveries is almost the same in the group who started treatment after the sixteenth week as in the group who started treatment prior to the sixteenth week. The value of treatment started prior to the sixteenth week is to be found, however, in the prevention of fetal deaths due to syphilis and in a marked decrease in the tendency to transmission of the disease. The decrease in fetal deaths where treatment is started early is shown by the absence of

fetal deaths in the group who started treatment prior to the sixteenth week in contrast to a 7 per cent incidence of fetal deaths in the group who started treatment after the sixteenth week. The decreased tendency to transmission is well shown by a 2.7 per cent incidence of live babies with syphilis in the group starting treatment before the sixteenth week in contrast to a 13.9 per cent incidence in the group starting treatment after the sixteenth week.

Treatment given even late in pregnancy, during the last trimester only, is of value. Such late treatment helps to prevent the transmission of the disease. This is shown by the fact that 62.1 per cent of the babies born to mothers who received late treatment were alive and free from the disease compared with only 12.3 per cent of the babies born to untreated mothers. While the incidence of live syphilitic babies was almost the same in the untreated group as in those patients who received late treatment only, such treatment reduced the frequency of the serious ravages of the disease, namely, macerated stillbirths, and neonatal deaths. This is shown by the fact that there was an incidence of 3 per cent of macerated stillbirths in the group with late treatment compared with 29.2 per cent in the group without treatment. Likewise, the incidence of syphilitic neonatal deaths was reduced to 1.5 per cent from 24.6 per cent. Also the incidence of prematurity was reduced to one-fourth by late treatment.

REACTIONS TO THE ARSENICAL INJECTIONS

While the arsenical is unquestionably the most valuable drug in the prevention of the transmission of infection from mother to offspring, its use is not attended without untoward reactions. The results of the Cooperative Clinic Series³ are used for comparison. There were 11.77 gastrointestinal reactions per thousand injections as compared with 10.92 in the Cooperative Clinic Series dealing with pregnant women and 8.52 in nonpregnant women. Nitritoid reactions were encountered twice as often in the present series. Also a very marked increase in pruritus occurred, namely, 10.01 per thousand injections compared with 0.87 per thousand in the pregnant group of the Cooperative Clinic Series and 1.78 per thousand in the nonpregnant group. A total of 27.08 reactions per thousand was found in the Bellevue series, a higher incidence than that encountered in the larger Cooperative Clinic Series. Of the severe reactions, crustaceous dermatitis was encountered with almost the same frequency in all the groups. Icterus, however, was very much more frequent in the Bellevue series, there being 7.07 per thousand injections in this series whereas there were only 0.62 per thousand in the group of pregnant women and 1.12 per thousand in the nonpregnant group of the Cooperative Clinic Series. Two deaths occurred or an incidence of 1.17 per thousand injections, while no deaths were encountered in the Cooperative Clinic Series. One of these deaths was a very typical arsenical encephalorrhagia; this condition has also been reported by Beck,⁴ Plass,⁵ Schumann,⁶ and Kuhnel.⁷ It resembles specific toxemia with convulsions and may be readily mistaken for it. Its onset frequently occurs after the second or third injection during the latter part

on glass slides for direct examination. Budding yeast cells were seen in these smears in a high percentage of those cases in which cultures were subsequently positive. The cultures were incubated at room temperature. Since bacteria frequently develop on Sabouraud's medium, fungi when found were checked for purity by inoculating Sabouraud's acid dextrose broth and streaking a blood agar plate from this broth culture. We believe that some of the irregularities of carbohydrate fermentation noted by other observers may be due to the presence of two or more species of fungus on the original Sabouraud's slants or to an occasional bacterial contaminant. Blood agar, although not an ideal medium for the development of yeast-like fungi, is a very useful substratum for colony differentiation.

The following technique which was developed by empirical methods enabled us to identify all 68 strains studied. The procedures necessary for identification were:

1. Colonies on Sabouraud's dextrose agar were transplanted to Sabouraud's acid dextrose broth, incubated at 37° C. for forty-eight hours and the type of surface growth noted.

2. A beef extract blood agar plate, pH 7.4, was streaked from this Sabouraud's broth culture after shaking the tube to resuspend the sedimented organisms. These plates were incubated at 37° C. for ten days. Although most colonies developed well in three or four days certain types of monilia showed typical colonies only after longer incubation. If bacterial colonies appeared or two species of fungi were recognized, a single colony was selected and inoculated into another tube of Sabouraud's broth to observe the type of surface growth of the pure culture.

3. A single well isolated colony was picked from the blood agar plate and planted on a second Sabouraud's dextrose agar slant. After incubation either at room temperature or 37° C. some of the growth was transplanted to a sterile carrot plug which was subsequently examined at frequent intervals for evidence of ascus formation.

4. A beef extract dextrose-free agar slant was inoculated from the Sabouraud's agar slant which was used as inoculum for the carrot plug. This culture was incubated at 37° C. for twenty-four hours and subcultured 2 or 3 times. The most recent transplant was used to inoculate the various carbohydrate broths, milk, and corn meal agar slide cultures.

5. The carbohydrate fermentation reactions were tested by inoculation of beef extract broth containing 1 per cent of fermentable substance. Beef extract broth containing brom-thymol-blue was titrated to pH 7.2 before autoclaving at 15 pounds' pressure for twenty minutes. After cooling, the carbohydrate solutions, sterilized by filtration, were added. The inoculum consisted of a saline suspension of the scanty growth on beef extract agar. The growth was washed off in 1.0 c.c. saline and 0.1 c.c. quantities were pipetted into the various carbohydrate broths and milk.

6. Corn meal agar was prepared as described by Benham² and a slide culture made by flooding a sterile slide with the molten medium. After hardening, the agar was inoculated by making a heavy streak the length of the slide, splitting the medium. The inoculum always consisted of material from the beef extract agar slant. The slides were incubated at room temperature for several days in sterile moist chambers. After mycelial growth had occurred the slide was dried in the air, and fixed and stained with lactophenol and cotton blue.

7. Agglutination tests with immune rabbit serums were done with most strains.

None of the 68 strains produced asci on carrot plug and 9 failed to develop mycelia on corn meal agar. These 9 strains were classified as cryptococci and corresponded to Group I as described by Benham.⁷ The remaining 59 strains, which produced mycelia, were considered species of the genus *monilia* as this genus is generally interpreted in medical literature: i.e., yeastlike cells which reproduce by

showed no change in their reactions with the varying amounts of treatment as indicated. There were however, 3 or 2.7 per cent of the patients who showed a more strongly positive reaction post partum after having received moderate or little of the arsenical and bismuth. In the patients with early syphilis, most of whom showed secondary manifestations, a reversal of the Wassermann reaction occurred in a considerable proportion of the cases with comparatively small amounts of treatment. In the late latent cases, the largest percentage of cases showed no change in the Wassermann reaction because the period of observation and treatment ante partum was too short to bring about marked serologic changes.

CONCLUSIONS

1. The transmission of syphilis from mother to child can be prevented by early and adequate treatment given to the mother during her prenatal period.

2. Such treatment can be given most efficiently in a special Prenatal Syphilis Clinic properly equipped and staffed.

3. Ante-partum treatment will markedly reduce the incidence of premature deliveries.

4. With the decrease in premature terminations as the result of treatment there is a decreased incidence of breech presentations and a consequent decrease in operative deliveries.

5. Morbidity is very markedly increased in those untreated patients with early lesions. Most of these lesions were condylomata lata situated about the genitalia. Treatment in a similar group of patients reduced this incidence.

6. The incidence of maceration as well as the incidence of deaths due to syphilis was fifteen times higher in patients who received no treatment compared with those who received treatment both before and during pregnancy.

7. The nontreated group yielded live babies who were syphilitic twelve times more often than the treated group.

8. It is never too late in pregnancy to bring about some good by the use of antisiphilitic therapy.

9. Arsenical therapy given the pregnant woman is not attended without risk. The gastrointestinal reactions, pruritus, and icterus lead the list in frequency. Mild reactions are encountered with almost equal frequency in white and colored patients but severe reactions are more frequent in the former group.

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of pregnancy and treatment is usually without avail. The other death encountered following the use of the arsenical likewise occurred after the third injection, but the findings were those of a diffuse parenchymal cellular degeneration predominantly cerebral, hepatic, and renal. There was a total of 9.41 severe reactions per thousand injections in the present series as compared with less than one-fourth that number in the Cooperative Clinic Studies dealing with pregnant women.

The difference in the results between the two series may in part be accounted for by the special alertness for such reactions in the Bellevue Hospital Clinic. Another factor is the disproportion between the sizes of the two series. Finally, the possibility of racial susceptibility to the arsenicals may account for part of the difference in the results. Mindful of this last possibility, a study was made of the reactions encountered in 149 white and 44 colored patients. The first group received 1,416 injections and showed an incidence of 27.55 mild reactions per thousand and 11.29 severe reactions per thousand. The colored group on the other hand, although the number is small, and only 282 injections were given, showed an incidence of mild reactions which was a little lower than in the white group, but there were no severe reactions encountered. Icterus was the most common of the severe reactions. Its determination clinically is difficult in the colored group unless the icteric index is done as a routine. However, if icterus had occurred, more likely than not in many instances further serious consequences such as acute yellow atrophy would have resulted with further treatment, so that it may be assumed that icterus as a reaction was probably very infrequent in this group.

STUDY OF THE WASSERMANN REACTION FOLLOWING TREATMENT

Finally a study was made to determine the effect of ante-partum treatment upon the Wassermann reaction, dividing the cases into those with early syphilis, late syphilis, and latent syphilis, and using the maternal seven-day Wassermann reaction for comparison with the Wassermann reaction prior to the onset of therapy. There were 19 patients with early lesions practically all with secondary manifestations and all in the seropositive stage. In this group there was an incidence of 42.1 per cent of Wassermann reversals. These reversals followed the use of moderate-moderate or moderate-much treatment. There was a similar incidence of no change in the Wassermann reaction. Three patients or 15.8 per cent with varying amounts of ante-partum treatment showed a less strongly positive reaction post-partum. There were 6 patients with late manifestations whose Wassermann tests were followed, none of whom showed a complete reversal; one with moderate-moderate treatment showed a less strongly positive reaction, and 5 with varying amounts of treatment showed no change.

In the study of the latent cases with other than negative reactions to start, there were 7 reversals or 6.1 per cent brought about mostly with a moderate amount of the arsenical. There were 22 or 19.5 per cent who showed a less strongly positive Wassermann reaction after varying amounts of treatment. The largest number, namely, 81 or 71.7 per cent

TABLE II. PREGNANCIES

	GROUP I (PREVIOUS PREGNANCY)	GROUP II
Primiparas	83	19
Multiparas	317 = 801 preg.	152 = 590 preg.
Healthy children	128 or 16%	113 or 19%
Syphilitic children	118 or 14%	286 or 48%
Stillbirths	168 or 21%	78 or 14%
Miscarriages	120 or 16%	76 or 12%
Children with no data	267 or 33%	45 or 7%

children, 48 per cent definitely syphilitic. Another 26 per cent showed interruption of pregnancy before term with macerated fetuses. Another 7 per cent, or 45 of them, could not be followed, 14 of whom had previously died. Undoubtedly, some of those were syphilitic.

TABLE III. RELATIONSHIP OF EARLY AND LATE TREATMENT

MONTH OF PREGNANCY TREATMENT STARTED	NO SYPHILIS IN CHILD	SYPHILIS IN CHILD
2-4	31	1
5-6	47	3
7-9	58	13
Total	136	17

Table III shows that if the patient is treated early in pregnancy, there is very little syphilis left in the child. There was one syphilitic child out of 32 cases where treatment was started from the second to the third month of pregnancy, inclusive. There were 3 out of 50 patients who showed syphilis when treatment was started from the fourth to the sixth month, inclusive. Thirteen out of 71 patients, however, showed a certain amount of syphilis if the mother was treated only during the latter part of pregnancy. In all of those cases the congenital syphilis was very easily controlled by antisyphilitic treatment.

I would like to emphasize the necessity of long observation of these infants. One cannot say that there is no syphilis in these infants after a follow-up of only two or three months. I have seen quite a few cases of signs of syphilis appearing after four, five, six, or eight years. Latent syphilis would then become manifest in the form of an interstitial keratitis, a nerve deafness, or some other evidence of congenital syphilis. It is only by continued study over a long time that we can solve this problem.

DR. WALTER CLARKE.—There is a real need for the thorough investigation of syphilis as a complication of pregnancy such as Dr. Speiser has been carrying on at Bellevue Hospital. His results give almost 95 per cent of satisfactory pregnancies in syphilitic women where the patient had had treatment both before and during the pregnancy (94.7 per cent). These results are as good as have ever been obtained in any piece of work of this sort.

There is in this city no prenatal clinic which does not do routine serologic tests for syphilis. The real difficulty comes in two other respects, first, that the patients are not properly followed after having been discovered and sometimes are not kept under treatment. Second, routine serologic tests in pregnant women are not commonly done in private practice. In other words, the situation in this city is that women who go to prenatal clinics, which are commonly free, are given more scientific care, as far as syphilis is concerned, than those who go to private physicians and pay a fee for it.

In the clinics and hospitals a really fine piece of work is being done on the discovery of syphilis. The place where we are failing, and failing lamentably, not only

DISCUSSION

DR. WILLIAM T. DAILY.—The remarkable thing about the treatment of syphilis, in the pregnant woman, is the fact that fetal syphilis may be prevented and cured, even though our treatment fails to cure the mother. Salvarsan apparently is much more efficacious in fetal than in adult tissue.

Even in the late months if treatment is intensive, a fair number of nonsyphilitic children will be born and syphilis in the others can be more easily controlled. On the other hand, a well treated patient whose Wassermann remains negative before she becomes pregnant, should not be disregarded. In her case, the disease may be latent and at any time the fetus may become infected. The history of previous pregnancies is most valuable, and in some suspicious cases in which the Wassermann is negative, a provocative injection of arsphenamine has led to a positive serologic reaction.

TABLE I. GROUP 1, PRENATAL CASES FOLLOWED FROM FOUR TO FIFTEEN YEARS

NUMBER OF SALVARSAN TREATMENTS	NUMBER OF PATIENTS	OFFSPRING WITHOUT SYPHILIS	OFFSPRING WITH SYPHILIS	STILLBIRTHS	MISCARRIAGES	PERCENTAGE OF OFF- SPRING WITHOUT SYPHILIS	PERCENTAGE OF OFF- SPRING WITH SYPHILIS	PERCENTAGE OF STILLBIRTHS	PERCENTAGE OF MISCARRIAGES
1-3	125	85	18	15	7	68.0	14.4	12.0	5.6
4-6	133	120	11	2	0	90.5	8.4	1.5	0.0
7-9	85	73	6	6	0	86.0	7.0	7.0	0.0
10-12	33	32	1	0	0	97.0	3.0	0.0	0.0
13-15	16	15	0	1	0	94.0	0.0	6.0	0.0
16+	18	16	2	0	0	89.0	11.0	0.0	0.0
	410	341	38	24	7	83.0	9.0	6.0	2.0

DR. THURMAN B. GIVAN.—Table I represents a follow-up of the children of women who were treated prenatally. These patients have been observed for from four to fifteen years, and represent 410 pregnancies in which the patients were given varying amounts of neosalvarsan as well as either mercury or bismuth. It is easily seen from this chart that 341 of the 410 patients remained free from syphilis for from four to fifteen years after delivery. Those that received the least treatment presented the most syphilis. High percentage of stillbirths and congenital syphilis, occurred in those that received only one to three salvarsan injections prenatally. Dr. Speiser remarked that 15 doses would protect the baby and that is usually so. In the 18 patients of my series who received such treatments there were, however, two very definite syphilitic babies. These infants both had syphilitic meningitis, although both mothers were treated throughout pregnancy almost weekly from the second or third month of gestation. Both of these babies are well now, and their hydrocephalus has been easily controlled without any mental deficiency so far. It is a matter of conjecture whether or not the spirochetes in these two women belong to that strain which picks out the central nervous system in the infant.

Table II shows that these patients 83 of whom were primiparas and 317 multiparas, had had 801 previous pregnancies. There were only 128 or 16 per cent that showed no definite syphilis in the living children, although there was a 33 per cent incidence that could not be followed. As might be surmised, a great many of these children were married and were inaccessible, many others undoubtedly are dead. Of those that could be followed, 14 per cent showed syphilitic children. Another 37 per cent resulted in stillbirths or miscarriages. A second group were mothers of children with congenital syphilis in our clinic, 19 primiparas and 171 multiparas, having a total of 590 pregnancies. There were 19 per cent of healthy

ADMINISTRATION

We gave the following dosage: In patients under 130 pounds, we gave an initial dose of 9 gr. in 4 ounces of ether oil mixture per rectum (2.5 ounces of ether to 1.5 ounces of olive oil). No quinine was used in our ether oil mixture. For patients over 130 pounds, we gave 12 gr. in 4 ounces of ether oil mixture. We gave the medication as soon as the patient was definitely having regular pains and discomfort, regardless of the degree of dilatation of the cervix. The average degree of cervical dilatation at which the initial dose of medication was given in our 101 cases was, however, 4 cm. The average dilatation of the cervix at the time of the second administration of the drug, which was required in 29 cases, was 6 cm. At the time of the initial administration of the drug, the level of the presenting part varied from "engaging" to "midpelvis." If the labor was a long one and further medication necessary, we gave one-half of the original dosage in 3 ounces of ether oil. It was never necessary to give more than 21 gr. to any one patient, in divided doses, although we at times repeated the ether oil alone. No scopolamine was given to any patient in this series.

On admission, the patients were routinely given an enema of 2.5 per cent bicarbonate of soda solution. This was chosen in preference to a soapsuds enema, because it was felt to be less irritating, and helped to lessen the possibility of expulsion. The medication was given according to the usual technique for administering rectal ether, with the following exception: Only enough bland oil to fill the rectal tube, and eliminate air, preceded the medication and no oil followed it. The instillation was done rapidly between two pains, and a folded vaginal pad was held firmly against the rectum for fifteen to twenty minutes following the removal of the rectal tube. Using this method, we had little difficulty with expulsion of the medication, and prompt absorption seemed to be the general rule. The action of the drug was often almost instantaneous, but as a general rule sleep ensued within twenty to thirty minutes. Four patients out of 101, expelled a part of the instilled solution. We endeavored to wait one-half to three-quarters of an hour after expulsion of the admission enema before giving the rectal medication. Following the medication, an occasional patient complained of a burning sensation in the rectum. This subsided within five to ten minutes at the longest.

OBSERVED CASES

Our series comprised 101 cases selected from the routine ward admissions. We endeavored to choose only the patients in whom we felt delivery was not imminent. The patients comprised 77 primiparas, 21 multiparas previously delivered of one baby, and three previously delivered of two babies. Their ages ranged from 17 to 37 years, and they were all of the white race. Among these patients, there were 78 normal pelves, 5 simple flat pelves, 9 funnel-shaped pelves, 7 justominor pelves, and 2 justominor flat pelves. There were 3 breech presentations and 98 vertex presentations. The types of deliveries were as follows: 81 by low forceps, the majority of which were prophylactic; 14 spontaneous; 3 by midforceps; and 3 breech extractions. In the following estimation of the length of labor, it should be remembered that the length of the second stage of labor is shorter than the usual average in our cases. This is due to our routine use of perineotomy and low prophylactic forceps under gas anesthesia in all primiparous labors. The length of the third stage is also shorter than the average, due to the routine use of gas anesthesia and Credé expression of the placenta.

An analysis of our observations shows the following:

1. *The Drug Gave Complete Analgesia and Amnesia in Favorable Cases.*—

ANALGESIA		AMNESIA	
Excellent	75 cases (74%)	Excellent	68 cases (67%)
Good	11 cases (11%)	Good	19 cases (19%)
Fair	4 cases (4%)	Fair	3 cases (3%)
Poor	11 cases (11%)	Poor	11 cases (11%)

in New York City, but all through the country, is in the discovery of syphilis in private practice. You cannot expect to find syphilis in pregnancy in any large proportion of cases unless routine serologic tests are done.

DR. MORTIMER D. SPEISER.—Besides the false negative Wassermann reaction there is, of course, another possibility, namely the question of infection occurring late in pregnancy. For that reason several investigators interested in this phase of the work have recently advocated a routine Wassermann, not only at the time of the first admission to the clinic but also at a later date about the eighth month, in order to detect those patients who have acquired their infection during the course of their pregnancy.

We are fortunate at the present time to be able to do a precipitation test (Kline) as well as a Wassermann test on the patients in the prenatal syphilis clinic at Bellevue Hospital. One test, therefore, acts as a check against the other and we are looking for discrepancies occurring in either test.

A CLINICAL STUDY OF ACID ALURATE AS A RECTAL ANALGESIC DURING LABOR*

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THIS study was undertaken at Woman's Hospital on the Ward Obstetrical Service, over a period of five months. Acid alurate (allyl-isopropyl barbituric acid) is soluble in ether oil mixture for use in rectal analgesia. Our interest in the drug was aroused because of favorable reports of its use at Fifth Avenue and Lincoln Hospitals in this City. We had been routinely using nembutal (pentobarbital sodium) and scopolamine on the Ward Service with the occasional addition of rectal-ether-oil. We had experienced the usual difficulty with marked restlessness in many patients and the resulting nursing problem. We had also certain patients who vomited medication, and in whom rectal administration seemed more satisfactory. It seemed interesting, therefore, to study a drug which was soluble in the Gwathmey mixture and would necessitate one instillation only and to try to evaluate this drug as to: (1) Effectiveness in the production of analgesia and amnesia, (2) degree of restlessness and difficulty in control of patient, (3) toxicity in regard to the mother, (4) toxicity in regard to the baby, (5) effect on duration of labor, (6) length of duration of analgesia, and (7) effect on third stage of labor.

Because the use of the rectal route in giving medication is not ideal in all patients, we selected only cases where this method seemed advisable. We did not attempt to use it in cases far advanced in labor, with the head deep in the pelvis, or where delivery seemed imminent within one to two hours.

*Read before the Section of Obstetrics and Gynecology, N. Y. Academy of Medicine, May 25, 1937, at a Resident's Program.

4. *Toric Effects of the Drug on the Babies.*—Of the 101 babies delivered, there was one stillbirth of a hydrocephalic monster. The fetal heart in this case was not heard on examination at the time of admission, which leaves 100 children who were born alive and in good condition. The average weight of the babies was 7 pounds and 3 ounces with a variation from 5 pounds 9 ounces to 10 pounds. Of these 100 children, there were 90 who breathed spontaneously at birth and required no efforts of the obstetrician to initiate respiration. Eighteen babies included in the 90 had sufficient mucus or meconium or both in their respiratory passages to necessitate aspiration to relieve partial obstruction. Seventy-two babies or 72 per cent of the series breathed spontaneously without any stimulation. Ten of the 100 babies were definitely narcotized, but were easily resuscitated by the administration of a mixture of 10 per cent CO_2 and 90 per cent oxygen following aspiration of mucus.

Fourteen babies of the 100 delivered showed enough definite variation in the fetal heart rate to be classified as abnormal. Two showed marked slowing during the second stage, and at delivery were found to have a loop of cord tight around the neck and shoulder. Passage of meconium was also noted in these two cases. Of the remaining 12 babies, 11 showed a definite increase in the fetal heart rate of 24 to 40 beats per minute immediately following the administration of the drug. In two of the cases, the rate of the fetal heart was observed to return to normal within an hour's time. In 9 cases, the fetal heart rate required two hours or more to return to the rate found prior to administration of the drug. There was one case in which the fetal heart became definitely irregular in rhythm during very forceful second stage pains. This arrhythmia was considered to be due to pressure exerted on the fetus by the strong uterine contractions. Of the 11 babies showing an increase in rate of the fetal heart, only one showed a definite arrhythmia which was considered to be due to the drug. All babies appeared normal in development at birth, and were discharged from the hospital in good condition.

There were 11 cases of vertex presentation in which there was a definite passage of meconium prior to delivery, but only one required resuscitation with CO_2 and oxygen and aspiration. The remaining 10 were aspirated although they started to breathe spontaneously.

5. *Effect on Duration of Labor.*—In consulting three textbooks on the average duration of labor we found: Davis in reviewing 5,600 cases gives the average total labor in primiparas as fourteen and one-half hours and in multiparas as eight hours and forty minutes. Curtis records seventeen hours as the average length of labor in primiparas, and twelve hours as the average in multiparas. Williams considered eighteen hours and twelve hours to be the average for primiparas and multiparas, respectively. In our series, the average time for the second stage should be shortened due to our routine use of prophylactic low forceps and perineotomy. Even considering this fact, it is seen that with the use of the rectal medication the total length of labor was definitely lengthened in our series. The average length of labor was eighteen hours and thirty-three minutes in 77 primiparas, and fourteen hours and thirty-five minutes in 24 multiparas.

It was interesting to note that the average time before delivery after the medication was given was approximately the same for both classes of patients, namely, being seven hours and thirty-four minutes for the primiparas, seven hours and twenty-eight minutes for the multiparas.

2. Degree of Restlessness, Noisiness and Difficulty in Control of Patients.—

Restlessness:

Completely narcotized	40	} 55	} 60	Excellent
Slight turning with pains	15			
Patients requiring two doses of medication		5	} 16	Good
Late second stage only		16		
Restless during pains, slept between pains		11		
Restless throughout		14		Poor

Noisiness:

Completely quiet	55	} 9	} 64	} 65	Excellent
Talkative first ½ hour after medication	9				
Requiring 2 doses			1	} 11	Good
Late second stage only			11		
Moaning with pains, slept between pains			16		
Noisy throughout			8		Poor

Ten patients were difficult to control all during their labors, and 12 patients required special watching during a part of their labors. The remaining 79 patients did not require the attention of a special nurse.

3. *Evidence of Toxic Effect of Drug on the Mother.*—An estimation was made of the changes in pulse rate, of respirations during labor, and of any abnormal sequelae following administration of the drug. The blood pressure was taken routinely before the drug was administered, and following delivery and anesthesia. No marked change in the blood pressure was noted in any case. No maternal mortality.

In an analysis of the pulse rate, 71 patients showed no change in the estimation as taken on admission, following medication and throughout labor. Of the remaining patients (30), 23 showed an average increase of 15 beats per minute following the first instillation of the drug, and 3 showed an average decrease of 15 beats per minute. Four patients showed no change following the first medication, but were included in the series because of a change in pulse rate after a second instillation of the drug. Of the 29 patients in whom it was necessary to repeat the medication, only 9 patients showed a change in pulse rate. Of these 9 patients, 7 showed an average increase of 25 beats per minute, and 2 showed an average decrease of 12 beats per minute.

In studying the effect of the alurate on the rate of respirations: 99 patients out of 101 revealed no change. Of the remaining 2 patients, one developed a rather severe coughing attack during the second stage which soon subsided with change of position. The other patient developed a dyspnea with slight cyanosis, and rather clammy skin following the medication, which subsided spontaneously after one-half hour's duration.

A diplopia of forty-eight hours' duration accompanied by physiologic cupping of the disks, developed in two patients, and a mild diplopia of twelve hours' duration developed in one patient. In each of these 3 patients, the diplopia subsided spontaneously. One patient on the fourteenth post-partum day developed diplopia with other unusual neurologic symptoms, the etiology of which was not directly associated with the medication. This patient also recovered spontaneously. Both her neurologic signs and diplopia developed four days after the onset of a hyperpyrexia due to acute pyelonephritis. The remaining 97 patients showed no ocular symptoms or signs.

Ninety-eight patients were free from abnormal desire for sleep following delivery, while one patient slept for thirty-six hours, and two patients were partially narcotized for twenty-four hours. A tabulation of the remaining sequelae occurring in the 101 patients follows:

Three patients had a post-partum hemorrhage estimated at 300 to 400 c.c.

Two patients had adherent placentas requiring manual removal.

One patient had a slight headache of twenty-four hours' duration.

One patient developed phlebitis on the sixth post-partum day which subsided rapidly.

One patient developed acute pyelonephritis, mentioned above as also having diplopia.

X-RAY DIAGNOSIS OF PLACENTA PREVIA*

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UDE, Weum, and Urner,¹ in 1934, suggested a method for the diagnosis of placenta previa by x-ray and, in 1935,² reported 35 cases in which the method had been employed. Since the lower uterine segment and the two peritoneal layers of the bladder reflection are the only structures between the urinary bladder and the fetal head, it is their belief that a cystogram in the presence of placenta previa will show an abnormally wide space between the head and the bladder. Their technique is as follows: A catheter is inserted into the urinary bladder and, after withdrawing the urine, 40 c.c. of a 12½ per cent solution of sodium iodide are injected. After removing the catheter, an anteroposterior plate is then taken, with the tube centered over the mid or lower abdomen. In their experience, the normal bladder shadow conforms nicely to that of the head, with an intervening space of approximately 1 cm. In the presence of central placenta previa, there is seen a much wider separation of head and bladder shadows throughout. On the other hand, in partial placenta previa, a wider separation is observed on one side, the side of the placenta. They feel that, by this means, placenta previa can be diagnosed or ruled out with a high degree of accuracy, except in breech and transverse presentations.

On the Obstetrical and Gynecological Services of The Long Island College Hospital and of the Long Island College Division at Kings County Hospital, we have taken x-ray films of 90 cases admitted with bleeding in the last trimester of pregnancy. Of these, 19 revealed the presence of breech or transverse presentation in which, as above stated, this method is of no value. These, accordingly, are not considered in this report.

Thus we have 71 cases of last trimester hemorrhage examined by x-ray. The diagnosis was correct in 63 or 88.7 per cent of the cases, and incorrect in 8 or 11.3 per cent.

In the series are 17 cases of placenta previa. Of these, the diagnosis was correct in 13 or 76.5 per cent and incorrect in 4, or 23.5 per cent. One of the errors is seen in Fig. 1. This patient, a nullipara, was admitted at eight and one-half months, with a history of painless, causeless hemorrhage. The plate shows an apparently normal relationship between head and bladder shadows. Yet, at cesarean section, placenta previa was unquestionably demonstrated, lying to the right and posteriorly.

CONCLUSIONS

Although this series of cases is small, our results would seem to indicate that this combination of drugs is reasonably effective in producing adequate obstetric amnesia and analgesia. As far as could be determined, there were no serious toxic reactions in either mother or child. In 25 mothers and 11 babies, there was a definite increase in the rate of the heart which directly followed the administration of the drug. This was temporary in character, and seemed to be due to the acid alurate. There was no constant definite effect on blood pressure or respirations and no increase in blood loss due to the drug. The duration of labor was definitely increased, and we feel this to be the major objection to the use of this combination of drugs.

Since our primary aim was to find a more effective analgesic than our own routine of pentobarbital sodium and scopolamine with ether oil, we cannot say that we have succeeded. In comparison to a similar series of 100 cases at the Boston Lying-in Hospital (Irving, Berman and Nelson), a combination of pentobarbital sodium and scopolamine produced 86 per cent complete amnesia and no failures. In our series there was an excellent amnesia in 67 per cent, and a partial amnesia in 22 per cent. Failure resulted in 11 per cent of our cases. On the other hand, our frequency of pronounced excitement was 14 per cent as compared to 16 per cent at the Boston Lying-in.

In regard to the effect on initial respiration in the infant, there were 72 per cent who breathed spontaneously at birth, without any artificial stimulation, as compared to 63 per cent in the Boston Lying-in series.

Our greatest objection to the use of acid alurate in rectal ether oil was the increase in the duration of labor of approximately two hours in primiparas and five hours in multiparas as compared to the standard textbook estimation.

We wish to express our appreciation of the cooperation given us by the Nursing Department of the Woman's Hospital and also to Hoffman-LaRoche Incorporated who furnished us with the drug.

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The injection treatment of varicose veins of pregnancy is a simple, safe procedure which gives better results than other methods. It should be used during pregnancy in preference to waiting until after delivery. Its use should be restricted to varicosities which are causing discomfort or pain or which may endanger the life of the patient at the time of delivery.

J. P. GREENHILL.

budding and by the formation of a mycelium, but which do not produce asci or aerial hyphae. Although the name *monilia* is invalid according to rules of botanical nomenclature, we have retained it in order to avoid the confusion that invariably follows changes in terminology. We have adopted the same species terminology as was used by Benham.²

The strains isolated from the vaginal tracts were identified as follows:

<i>Monilia albicans</i>	19 strains
<i>Monilia parapsilosis</i>	3 strains
<i>Monilia candida</i>	4 strains
<i>Monilia Krusei</i>	4 strains
<i>Monilia stellatoidea</i> n. sp.	29 strains
<i>Cryptococcus</i> sp.	9 strains

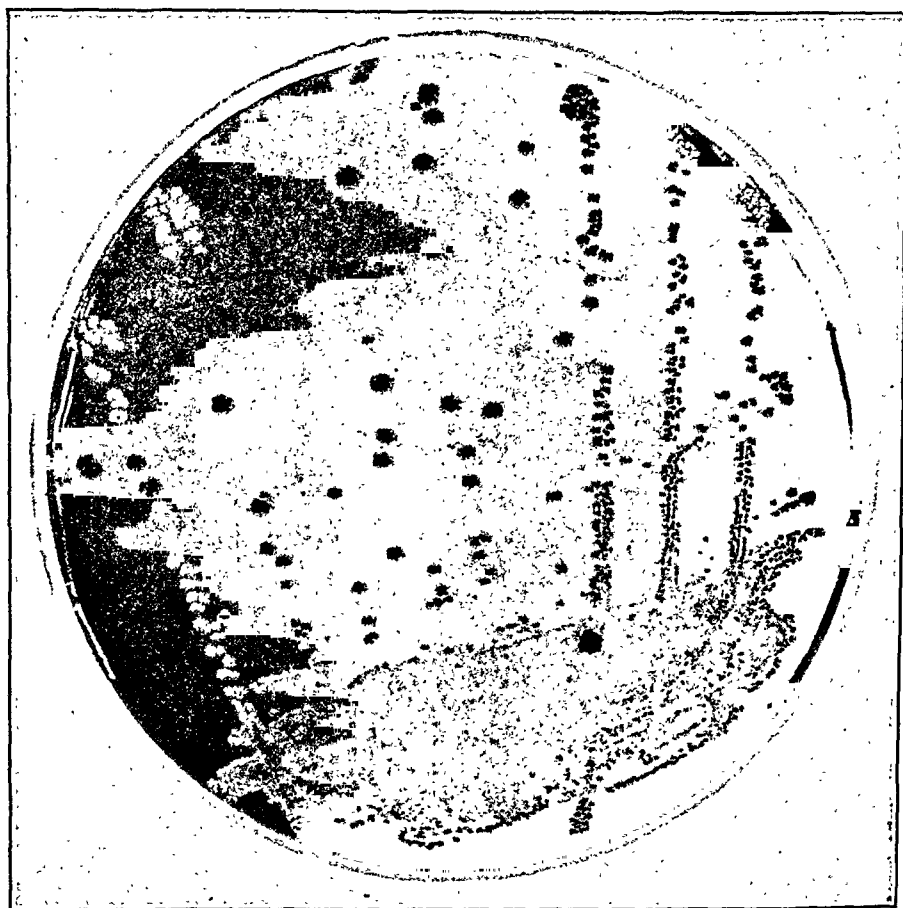


Fig. 1.—Colonies of *M. albicans* on beef extract blood agar pH 7.4, incubated at 37° C. for ten days.

CULTURAL CHARACTERISTICS

It should be emphasized that only gross differences in the type of growth in the various substrata are presented; minor variations not essential for identification are omitted. For example, the most obvious difference between *M. Krusei* and the other species of monilia on Sabouraud's dextrose agar is the flat dry growth of *M. Krusei* as compared with the moist creamy growth of the other species.

Growth in Sabouraud's Broth (48 Hours at 37° C.).—All species produced in this medium a growth which settled to the bottom of the tube leaving the supernatant

Of the 54 patients without placenta previa, the diagnosis was correct in 50 or 92.6 per cent, and incorrect in 4 or 7.4 per cent. Fig. 2 shows one of the incorrect diagnoses. This patient, a nullipara, was admitted with a history of painless, causeless hemorrhage at seven months. The plate reveals a distance much greater than normal between the head and bladder shadows. This would seem to be highly



Fig. 1.—Apparently normal relationship between head and bladder shadows indicating absence of placenta previa. Placenta previa, however, was found at operation.



Fig. 2.—Relationship of head and bladder shadows is suggestive of placenta previa. Placenta previa, however, was not present.

suggestive of central placenta previa; however, the patient did not have placenta previa. The roentgenologist was able to rule out placenta previa because he was able to visualize it in the fundus of the uterus. Thus, as suggested by Ude and Urner,² the coordination of their method with that of Snow and Powell³ may aid in establishing the location of the placenta.

Quite frequently, there is seen a distortion of the bladder to the right. We attribute this to the pulling of the bladder in that direc-

tion by the usual torsion of the uterus to the right. Fig. 3 shows a marked accentuation of this distortion. This patient, a para v, was admitted at eight months, with a history of having had two painless gushes of blood, estimated at a cupful each, one a week before, and one just prior to admission. The plate, though questionable, seems to suggest the presence of placenta previa on the opposite side. This patient did not have placenta previa.

In our experience, as the above statistics show, the method of Ude, Weum, and Urner may be helpful in the diagnosis of placenta previa. Its greatest value, however, lies in the fact that it enables us to rule out placenta previa with a fair degree of accuracy.

This study was undertaken in the hope that vaginal examination, with its attending dangers, might no longer be required in those patients in whom treatment by cesarean section was contemplated.

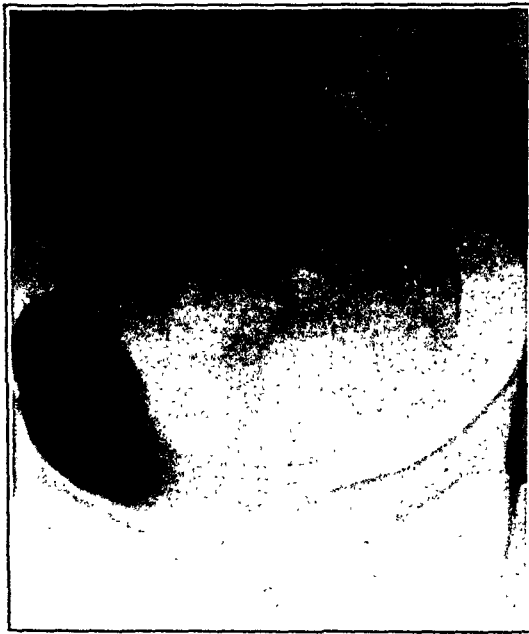


Fig. 3.—The greater distance of the head from the bladder on one side suggested placenta previa in this case in which placenta previa was not present.

While this hope has not been fulfilled, the x-ray has proved to be an aid in the diagnosis, and should be used only as such, in correlation with the history of the findings on abdominorectal examination.

CONCLUSIONS

1. Seventy-one cases of last trimester hemorrhage examined by x-ray are reported.
2. The diagnosis was correct in 88.7 per cent of all the cases.
3. Placenta previa was diagnosed correctly in 76.5 per cent of all the cases. Its absence was diagnosed correctly in 92.6 per cent of the cases.
4. The greatest value of the method is in ruling out placenta previa.
5. The method should be considered simply as an aid to the history and clinical findings.

Appreciation is expressed to Drs. A. L. L. Bell and Bernard Ehrenpreis, Roentgenologists at The Long Island College Hospital and at Kings County Hospital, respectively.

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20 LIVINGSTON STREET

DISCUSSION

DR. STANLEY C. HALL.—I have seen several cases in which there was a space between the presenting part and the bladder, and they were proved not to be cases of placenta previa. I think one may say that where there is a space it may or may not be placenta previa, but if there is no space it is not placenta previa.

DR. CAMERON DUNCAN.—This method has considerable value in cases that have been definitely diagnosed by vaginal examination. Where the cervix is dilated three or more fingers' and is covered by placenta, and a Braxton Hicks version is to be done, the cystogram shadow tells definitely to which side the greater portion of the placenta lies. Generally it lies more to one side than the other. Then one can go through the thin side of the placenta and cause less placental destruction with a better chance of a living baby.

DR. ALFRED C. BECK.—Although the pictures show some difficulty of diagnosis, I think there is no question but that this method is of very great value when taken in conjunction with the symptoms and possibly the findings on rectal examination, because it gives one more bit of information that should be very helpful.

To my mind, the worst case in the group was that one in which the head shadow conformed very nicely to the bladder shadow and the bladder was thinned out (Fig. 1). That was a case which most of us would regard as negative for placenta previa.

DR. FRANK P. LIGHT.—We were unable to make a diagnosis of the case illustrated in Fig. 1. The bladder very nicely conformed to the head except for one bit which was off to one side and seemed to be separate from the bladder shadow. Dr. Bell examined the plate and interpreted it correctly, saying that the placenta was posterior on that side and apparently gave rise to the separate shadow, but as far as we were able to tell, it was a negative plate.

Duncan, J. H.: *Neo-Natal Mortality (A Study of an Eleven-Year Period of Obstetrics in a Small City)*, *Canad. M. A. J.* 37: 474, 1937.

A neonatal mortality of 6.51 per cent is reported for Sault Ste Marie, Ontario, in the 6,954 deliveries from 1926 to 1936. Two-thirds of these deaths are ascribed to stillbirth or prematurity. The author feels that in order to prevent neonatal deaths more accurate information must be obtained by autopsy concerning the actual cause of death. The importance of correct diagnosis in syphilis, intracranial hemorrhage, asphyxia and aspiration pneumonia is emphasized.

CARL P. HUBER.

Latz, L. J., and Reiner, E.: *Failures in Natural Conception Control and Their Causes*, *Illinois M. J.* 71: 210, 1937.

The authors have accurately kept records of 379 women who had natural intercourse 15,924 times during the sterile period without occurrence of a pregnancy. In opposition to these confirmatory cases, few failures are recorded.

The authors conclude that at least 57 of the 59 apparent failures were not due to defects of the method of natural conception control, which is practical and reliable.

J. P. GREENHILL.

VESICOVAGINAL FISTULA

HARRY KOSTER, M.D., F.A.C.S., BROOKLYN, N. Y.

(From the Crown Heights Hospital)

NOT all vesicovaginal fistulas need to be operated upon through the vaginal route, because it will be found that certain of them are much more accessible abdominally. Accessibility is an important factor in free mobilization of the tissues surrounding the cicatrix, thus powerfully influencing the outcome of the operation, and should therefore receive consideration. Then the approach will be fitted to each fistula rather than all fistulas fitted to one approach.

In the past three years we have operated upon five patients with vesicovaginal fistulas. These amply illustrate the problem of abdominal versus vaginal therapy, so that no mention will be made of our other similar experiences. Of these five cases, one followed labor and the other four were the result of gynecologic operations. With improvement in the obstetric care of women on the one hand, and the marked increase in operative treatment of pelvic disorders on the other, it is not surprising to find a complete reversal of the ratio of obstetric to surgical causes of vesicovaginal fistula today as against that which prevailed even so short a while back as fifteen years ago. In those days, obstetrically-produced fistulas were relatively much more common. (Rawls,¹ Saenger,² Frank,³ Judd,⁴ Emmet.⁵)

For an excellent, although brief, historic review of the subject, reference should be made to the paper by Norman F. Miller.⁶

CASES

CASE 1.—E. S. (No. 22361), aged 65 years, admitted June 20, 1934, complaining of continuous urinary incontinence and a lump in the lower abdomen, increasing on standing and diminishing in the recumbent position. Her menopause had occurred fifteen years ago. Twelve years ago the patient was operated upon for prolapse, an abdominal and vaginal operation being done. Immediately after the operation she developed incontinence which has persisted since. About two months after the operation she noticed a lump in the lower abdomen which increased in size with the years. It protruded markedly in the upright position, but disappeared upon lying down.

There was a median lower abdominal scar of a previous laparotomy with a large mass protruding through it which could easily be reduced. Pelvic examination revealed a relaxed perineum with a small median perineal scar, a patulous urethral opening and a moderate cystocele. The cervix and the uterus were absent and there was a small opening from the vagina into the base of the bladder at a point where apparently the cervix formerly was, through which urine flowed. On coughing, there was considerable prolapse of the anterior and posterior vaginal walls and vault.

Operation June 21, 1934, began vaginally by exposing the fistulous tract from the vagina into the bladder, making a large incision in the vaginal mucous membrane with the fistulous opening in the center. The incision extended between 3 and 4 cm. in length and the vaginal flaps were dissected widely to either side, through which the base of the bladder could very easily be completely mobilized. The opening in the bladder was closed by two successive purse-string sutures without tension because

of the previous free mobilization. The redundancy of vaginal flap was excised and closed with interrupted chromic No. 0 sutures. An oval incision was then made on the abdomen around the hernia, excising the skin and exposing the fat. The fat was excised and after separation, the fascia was lapped by mattress sutures in two layers, the right side being pulled over the left. The skin was then closed with black silk sutures, a mushroom catheter was passed into the bladder and left in for eight days, the catheter being irrigated daily to prevent incrustation.

The patient made an uneventful recovery and was discharged in sixteen days, completely free from incontinence. She was seen again on May 17, 1937, at which time there was no recurrence either of incontinence or of the hernia.

CASE 2.—R. D. (No. 23991), aged 59 years, admitted Dec. 4, 1934, complaining of continual incontinence. Patient had had a hysterectomy performed eight months before admission and several days after the operation she began complaining of continual escape of urine from the vagina, with burning and scalding sensation over the vulva. There was a scar in the abdomen from the previous operation, but no hernia. There was a marked redness of the vulva and vaginal wall, and a small fistulous opening from the anterior vaginal wall into the bladder at a point corresponding to what was formerly the junction between the anterior bladder wall and the cervix. The hysterectomy had been done for prolapse, and there was a longitudinal scar on the anterior wall where operations for cystocele and rectocele had been performed. She was told that she had developed an infection of the vaginal wall and that a portion of the bladder had sloughed off, producing the fistula. The opening was 1 cm. long. The anterior and posterior vaginal walls were relaxed, and the vault descended on straining.

Operation was done Dec. 5, 1934, under spinal anesthesia. The anterior vaginal wall was split longitudinally and a mucous membrane flap dissected laterally so as to expose and make mobile a considerable portion of the base of the bladder around the fistula. The bladder opening was closed by two successive purse-string sutures with chromic No. 0 which inverted the former fistulous tract into the bladder. The redundant vaginal mucous membrane was excised and closed with chromic No. 1 in interrupted sutures. An indwelling catheter was left in the bladder for fourteen days.

She was discharged in twenty days, being completely cured of her incontinence.

CASE 3.—R. T. (No. 7507), aged 43 years, admitted Jan. 21, 1930, complaining of incontinence of urine since her last delivery two years ago. She had had a perineorrhaphy three years ago. Since her last pregnancy she complained of continuous leakage of urine through the vagina. There was considerable local irritation. There was a scar in the median line of the perineum of a previous operation, but there was still a slight rectocele and there was an opening from the vagina into the bladder on the anterior wall, almost 2 cm. in front of the cervix.

Operation was performed Jan. 22, 1930. A longitudinal incision on the anterior wall was made not quite 4 cm. long, with the fistula in the center of it, and two lateral flaps of vaginal mucosa were dissected backward, so as to mobilize freely the base of the bladder. The opening in the bladder was closed with two successive purse-string sutures of No. 0 chromic catgut, which inverted the fistula into the bladder. The redundant vaginal mucosa was excised and closed with interrupted chromic No. 0 catgut. A mushroom catheter was placed in the bladder and left in for eight days.

She was discharged in sixteen days cured of her incontinence.

CASE 4.—J. B. (No. 31096), aged 67 years, admitted Nov. 17, 1936, complaining of continuous incontinence. She had had her menopause fifteen years ago and a recurrence of vaginal bleeding twelve years later. Seven months ago a vaginal hysterectomy was performed for vaginal bleeding, immediately after which she had urinary leakage through the vagina continuously. There was a scar in the anterior vaginal wall, at the apex of which, high on the vaginal wall, there was a small opening through which a probe could be passed into the bladder. On cystoscopic examination, there was an opening about 0.5 cm. in diameter above the trigone, between the ureteral openings.

On Nov. 18, 1936, under spinal anesthesia, the abdomen was opened by a median lower abdominal incision. The rectosigmoid was found adherent to the vaginal stump. The adhesions were separated and the bladder mobilized. At the summit of the vaginal vault there was a small fistulous tract leading from the vagina into the bladder. The fistula was cut through transversely so as to separate further the base of the bladder from the vault of the vagina and to allow for a sufficient mobilization so that purse-strings of the hole in the base of the bladder could be done with a No. 0 chromic suture without undue tension. A second purse-string was placed around the first, thus inverting the bladder opening into the bladder lumen. The opening in the vagina was closed with No. 0 chromic and the bladder peritoneum was drawn across the vaginal stump and tacked down to the peritoneum in the posterior cul-de-sac. A mushroom catheter was placed in the bladder and was left in for eleven days.

The patient ran a febrile course for twelve days, the highest temperature being 103° F., on two successive days. She was discharged on the nineteenth day, completely free from incontinence.

CASE 5.—M. D. (No. 31730), aged 43 years, admitted Jan. 22, 1937, complaining of incontinence of urine for the past eight years. Eight years before, she had had a cervical repair for lacerations sustained at a delivery twenty-seven years ago. Immediately after the operation she began voiding urine through the vagina and was told that she had a vesicovaginal fistula. An attempt at repair was made four years ago, following which she had five transfusions, but the incontinence continued. From the vaginal examination it was apparent that a cervical amputation had been done. There was a small fistulous tract situated at the point where the anterior wall joined the stump of the cervix, which led directly into the bladder. Cystoscopic examination revealed a patulous tract in the middle of the trigone, midway between the ureteral orifices.

Operation on Jan. 23, 1937, under spinal anesthesia, consisted of a median lower abdominal incision. The uterus was liberated from a mass of adhesions of the omentum and sigmoid, the bladder reflection of the peritoneum was cut away, and the bladder was pushed off the anterior surface of the uterocervical junction, and the tissues between the bladder and uterus were separated by sharp dissection down to the fistulous tract. This was then cut through completely and the bladder further mobilized, so that the entrance for both ureters could be seen, as could also a considerable portion of the anterior wall, because the bladder and the vagina were completely separated by dissection. The opening in the bladder was then purse-stringed by two successive layers of No. 00 chromic suture, invaginating the fistulous tract into the bladder lumen. The vagina was closed with one layer of No. 00 chromic suture, and the bladder was then tacked back to its original position by sewing down the bladder reflection of the peritoneum to the uterus. A mushroom catheter was inserted into the bladder through the urethra. The catheter was removed in seven days and the patient discharged on the fourteenth day, completely dry.

She was seen again two months later, and it was verified that the incontinence no longer existed.

The five cases cited are illustrative of the problem as it is ordinarily encountered and a fairly large experience since 1919 has resulted in the development of certain principles, adherence to which, it is believed, will simplify the treatment and improve the results. It has long been known that one of the secrets of the successful operative procedure is good mobilization of the bladder. The only hindrances are inaccessibility when the fistula is high in the vault as after hysterectomy or the fear of encroachment upon the ureter. Such encroachment without recognition is possible only in the vaginal approach, where exposure is limited and dissection necessarily "blind." If such obstacles are expected, because of the location of the fistula, then by all means the abdominal route should be chosen. By this approach the base of the bladder may easily

be reached and freely mobilized so as to expose even the entrance of the ureter into the bladder and remove the fear of inclusion of the ureter in the suture used for closing the bladder opening. The vaginal route is a satisfactory one in lesions lower on the anterior vaginal wall which can easily be approached, either because of considerable relaxation of the vulva, or the utilization of an episiotomy in selected cases, or by traction on a retained cervix, or even by the use of traction sutures placed through the vaginal mucosa a short distance away from the vaginal opening of the fistula.

Where the abdominal route is chosen, the danger of soiling the peritoneum when the fistula is open and some urine escapes, has been grossly overestimated and should not be a deterrent to the employment of this route in cases which would otherwise be more favorably treated by it.

To sum up, the surgical approach should never be arbitrarily fixed, but should be fitted to the case, the desideratum being the maximum amount of mobilization of the bladder. It becomes easily understandable, then, the nearer the fistulous opening is to the vulva, the easier it is to approach it vaginally. The higher in the vault the fistulous opening is, the more readily is it approachable abdominally and the more successfully can mobilization be accomplished.

With good mobilization accomplished, the problem of suture material is immediately simplified. Silk has the disadvantage that, if buried, it may become infected and work its way into the bladder, either establishing a new fistulous opening or becoming incrustated with crystalline deposit and developing a calculus. Fine chromic sutures will hold the tissues in good apposition long enough to get complete healing if the mobilization allows of their placement without tension. On the other hand, given insufficient mobilization, any kind of wire sutures will cut through just as readily as chromic sutures. What is needed is approximation of the tissues by a suture under such tension that it will not cut through the tissues which it is expected to hold. Long duration of such an approximation is not necessary, because healing occurs rapidly. The failures result from the cutting through of the suture, because the tissues which it is attempting to keep in approximation, are under too great tension, as a result of insufficient mobilization.

The direction of the incision in the anterior vaginal wall for the dissection of flaps of vaginal mucosa away from the bladder so as to mobilize the latter, is not an important matter. The direction should be chosen for ease of manipulation and not with a view to sewing vaginal mucous membrane in a direction opposite to the bladder wall. Such steps are totally unnecessary if, again, the mobilization has been complete.

Methylene blue should not be used in the bladder for the identification of the fistulous tract. It very quickly discolors and obscures all the surrounding tissues. This is particularly true when the abdominal route is chosen. It is comparatively simple to recognize the fistulous tract by its appearance and by the way the tissues in the neighborhood cut. In its immediate neighborhood, the scar is very dense and unyielding, whereas a few millimeters away the tissues separate very easily.

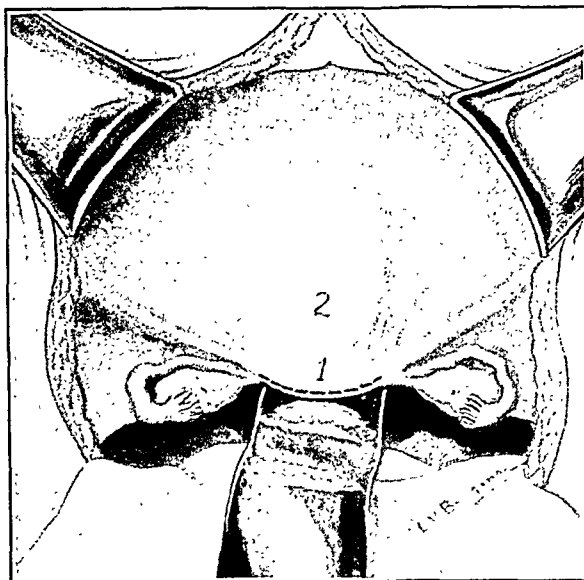


Fig. 1.—Pelvis after hysterectomy when adhesions have been separated. 1, Stump of cervix or vagina covered by peritoneum, 2, Bladder. Fistula is hidden by adhesions between stump and bladder. Dotted line marks site of incision of peritoneal flap which is to be pushed back to expose the vaginal wall and the fistula.

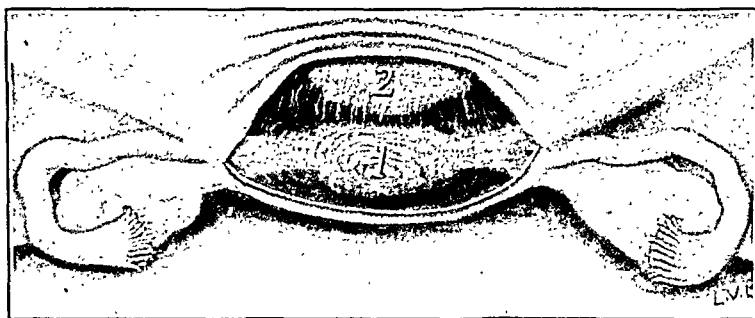


Fig. 2.—Peritoneal flap pushed back exposing 1, stump and 2, bladder. Between the two is seen a bit of the anterior vaginal wall before the fistula is exposed. As the bladder is pushed off the vaginal wall, the fistula will be brought into view.

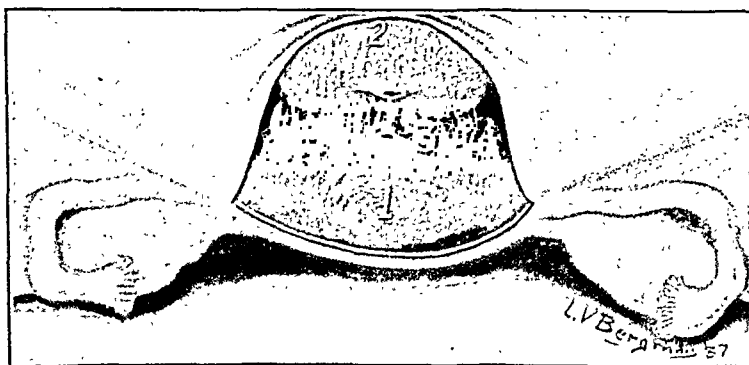


Fig. 3.—The bladder (2) has been pushed off the vaginal wall (3) exposing the fistula which is seen cut across. Purse-string sutures then close the openings into the bladder and vagina after which the peritoneal flap is sutured back in its original position over the cervix (1).

In doing the operation by the vaginal route, the dissection should be as extensive, if necessary, as one would make it in doing a cystocele operation. After free mobilization, the inversion of the opening into the bladder by purse-string sutures and the approximation of the vaginal flaps is easily accomplished.

Through the abdominal route, after the peritoneum is opened, the procedure depends upon whether or not the uterus has been removed at the preceding operation and, if the uterus has been removed, whether or not the cervix has been retained. Manifestly, if the uterus has not been removed, it is much easier to orient oneself. Under such circumstances the peritoneal fold which loosely passes from the posterior aspect of the bladder to the anterior surface of the uterus is incised transversely at the junction with the uterus and the bladder is pushed forward. It is found that the peritoneal reflection will peel off easily on both lateral sides but not readily in the median line. This is normally true because of the attachment of the pubovesical ligament in the median line but, in these cases, it is exaggerated because the fistula is found in most instances to be in the median line. Since the fistula is surrounded by a dense layer of scar tissue which is unyielding, there is resistance to the attempt to push the peritoneum and bladder off the uterus. The separation laterally, however, can be carried out to a considerable extent. As the peritoneum is pushed down, the bladder is carried along with it on the lateral side and, by sharp dissection, the separation is continuous towards the median line so as to isolate more definitely the tubular cicatricial tissue around the fistulous opening between the bladder and the vaginal wall. By this time the bladder peritoneum and the bladder itself have been pushed down to the vaginal wall laterally. Then, with sharp dissection, the fistulous tract is deliberately cut across. It is easily recognized by the granulation tissue and epithelium lining the tract. The separation is then continued more deeply in the median line between the base of the bladder and the vagina, and also further laterally so as, if necessary, to expose the points at which the ureters enter the bladder wall. By this time the base of the bladder has been thoroughly mobilized, so that it becomes a simple matter to invert the bladder portion of the fistulous opening, by a purse-string, into the bladder lumen itself and reinforce it again by another purse-string of No. 00 chromic suture. The vaginal opening is similarly treated and the bladder allowed to fall back into its original position. The edge of the peritoneum, where the bladder was detached from the uterus, is now tacked back on the uterus again and all the raw surfaces thus covered with peritoneum. The abdomen is closed. (In case of doubt, preliminary catheterization of the ureters may be used as a guide to their identification at operation.)

This is the technic which was employed in Case 5. If, however, the previous operation has been a hysterectomy, either total or subtotal, the procedure is slightly different. Under such circumstances the point of attachment of the loose peritoneum, as it extends from the bladder across the anterior cul-de-sac over to take its firm attachment on the uterus, is no longer utilizable as a landmark. Then the operation is done as in

Case 4. Whatever adhesions exist are to be separated until the stump of the cervix or the stump of the vagina is recognized and the peritoneum, which has been utilized to cover such a stump, is then separated over the posterior aspect of the stump and lifted from it so as to avoid accidentally entering the bladder from above. Such an accident is, of course, easily avoidable if one is on the lookout to recognize the muscular tissue of the bladder wall. The bladder is then separated from the anterior wall of the retained cervix or the anterior wall of the vagina, laterally at first because of the greater ease, and then in the median line when the cicatricial tissue of the existing fistula has been recognized, in very much the same manner. The rest of the operation proceeds as described above.

This method of approach is believed to be an improvement upon that of Legueu⁷ whose operation is planned on the assumption that the fistula is always in the median line. That occurs only in the majority of instances and a median incision does not provide for the exceptions. The transverse incision advocated here allows ready exposure of the tract irrespective of its relation to the median line and, incidentally, allows easier mobilization of the bladder than does Legueu's median line incision.

In the postoperative treatment, all that is necessary, besides the ordinary hygienic care given to any postoperative patient, is to maintain a free flow of urine through the retention catheter. When the catheter has a tendency to become blocked by incrustation, acidification of the urine and daily irrigations are advisable. It seems totally unnecessary to turn the patient on the abdomen to facilitate drainage from the bladder and to keep urine from having contact with the suture line, when it is remembered that the bladder is a muscular organ having considerable tone, surrounded by an intraabdominal pressure and always having its wall in apposition unless distended.

The transvesical suprapubic approach which has had a goodly number of supporters in the past, is subject to greater criticism than is the vaginal approach. Whereas through the latter it is possible to dissect off very large vaginal flaps for the purpose of mobilizing the bladder, through the transvesical approach any such attempt means more injury to the bladder tissue and a deliberate increase in size in the vesical portion of the fistula, both of which are not desirable.

The point on which it is desired to place special emphasis in this paper is that in many instances it is more likely that one will be hampered by using the vagina as an avenue of approach, whereas should the suprapubic route have been chosen, it would have been relatively simple to get adequate mobilization and a safe closure and cure.

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fluid relatively clear. *M. Krusei* and *M. candida* were the only species which produced any growth on the surface of the medium within forty-eight hours. All strains of *M. Krusei* produced a dry thin "collarlike" growth which extended up the sides of the tube to a distance of 5 or 6 mm. above the surface of the medium. Surface growth occurred with all strains of *M. candida* but the "collar" was narrower (2 or 3 mm.) and the surface film tended to be broken up by small bubbles of gas. Strains of other species occasionally produced surface growth irregularly if the tubes were incubated longer than forty-eight hours.

Colony Formation on Blood Agar (10 Days at 37° C.).—Characteristic colonies were obtained only if the blood agar plates were inoculated from Sabouraud's broth cultures. If subcultured from Sabouraud's dextrose agar or from beef extract agar, growth may or may not be typical.



Fig. 2.—Colonies of *M. stellatoidea* on beef extract blood agar pH 7.4, incubated at 37° C. for ten days.

M. albicans: Well isolated colonies were circular, approximately 1.5 mm. in diameter and the borders were smooth and regular. The surfaces were slightly convex and appeared dull grayish white (Fig. 1).

M. parapsilosis: These colonies were uniformly smaller than those of *M. albicans* (0.6 to 0.8 mm. in diameter) and more convex. The color was a definitely pearly white.

M. candida: This species produced the largest colonies on blood agar, attaining sizes of 2 mm. and more. The most characteristic feature was the wide "mycelial fringe" surrounding the colony. The mycelia grew only beneath the surface of the medium and formed a peripheral zone about 1 mm. wide around the entire colony. These colonies were grayish white in color but not as dull as the colonies of *M. albicans*.

vagina. Soda bicarbonate placed in the same size capsules were given to the same cases in rotation. Cervical biopsies were taken before and after each weekly exposure to the acid or alkaline as the case may be. In some cases, vaginal biopsies were also included.

All cervices, by hyperplastic change and disarrangement, subjected to a constant environment pH 6.5 to 7.5 showed some columnar epithelial proliferation and an acute cervicitis. All cervices subjected to a constant environment pH 4.0 to 4.5 showed some squamous epithelium returning to the cervix with a retreat of the columnar epithelium. I do not mean that we caused chronic papillary erosions to disappear, but the shift to more squamous epithelium was noticed. The simple erosions would show columnar epithelial retreat with squamous epithelium returning to the vaginal portions of the cervix after one to two weeks of constant acid environment, pH 4.0 to 4.5.

In the full report which will follow, the complete evolution of the various types of cervical erosions will be demonstrated. For the present, there is sufficient evidence that the vaginal pH alone can change the histologic picture of the cervix.

The cervix uteri is composed of the endo- and a vaginal portion. The endocervix is made up of columnar epithelial lined racimose glands which are bathed in an alkaline environment, pH 7.0 to 7.5. The vaginal portion of the cervix, which is covered with squamous epithelium, should be and is under normal circumstances in an acid environment, pH 4.0 to 4.5. This acid vaginal environment is produced by desquamation of the vaginal epithelium (esterin action) depositing acid fermentable material for fermentation by the Döderlein bacilli in the vagina. If the vaginal pH 6.5 to 7.5 is produced, the thin squamous epithelium of the vaginal portion of the cervix is destroyed, and the columnar epithelium from the cervical canal pushes out into this environment from whence it has come. Change the vaginal pH to 4.0 to 4.5, and we believe that the columnar epithelium will fall back into the canal environment and squamous epithelium will return to the vaginal portion of the cervix again. When the cervix has been lacerated exposing the canal, if the vagina is kept acid, columnar epithelium will retreat further up the canal, and squamous epithelium will cover the exposed endocervical portion.

In cases of papillary erosion of the cervix, the columnar epithelium has been piled up for so long that even when the squamous epithelium replaces portions of it, there can be no retreat of this hyperplastic tissue up the cervical canal. Structural removal of this tissue is indicated.

When infection is present within the vagina or cervix, the pH is always on the alkaline side, vaginal pH 5.5 to 7.5 (with one exception, e.g., fungus mycosis vaginitis, pH 3.5 to 4.0).

ON THE ETIOLOGY OF CERVICITIS

A PRELIMINARY REPORT

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THE histologic response in the cervix to the chemical environment in the vagina is the basis of the present study being conducted in the cervicitis clinic at the Washington University School of Medicine. Two years ago a report of a five years' study on the various surgical diathermy methods in the treatment of cervicitis was made. In May of this year at the Missouri State Medical Association meeting, I presented a paper on "Vaginitis and Cervicitis," concluding that the treatment for vaginitis was replacement therapy, and the treatment for cervicitis was removal therapy.

By replacement therapy is meant the addition of acid fermentable material to the vagina, which will maintain a vaginal pH 4.0 to 4.5 as limits. By removal therapy is meant the structural removal of the hyperplastic gland-bearing area of the endocervix. These two principles are fundamental in the management of the cervicitis-vaginitis syndrome.

The routine of the gynecologic clinic for the past year has been to place all patients with leucorrhea on acid fermentable material, and then to refer them to the cervicitis clinic following their next menstruation. The use of this routine has eliminated one type of cervical erosion.

Formerly, simple erosions, that is columnar epithelium replacing the squamous epithelium about the os of the cervix, constituted at least one-third of all the cases. Now, none of these cases are seen. Only the advanced erosions of the papillary type are now observed. This observation was so constant that in order to study again the simple erosion, we had to ask that such cases be sent for study before being placed on our new acid replacement therapy.

The next step was to take different types of cervixes: (1) acute cervicitis, (2) chronic cervicitis, (3) postpartum cervixes at six weeks, (4) simple erosions, (5) papillary erosions, and (6) normal cervix, and subject these cervixes to a constant acid fermentable environment, such as beta lactose 80 per cent, boric acid 20 per cent in a large gelatin capsule, which would contain from 11 to 12 c.c. of this powder by volume, the patient inserting these capsules daily well up into the

DUPLICITY OF UTERUS AND VAGINA

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ALTHOUGH knowledge of a double uterus dates back to 1681 when Dionis (Salacz, 1933) published a case of simultaneous pregnancies in both halves of a double uterus, there has been a paucity of articles on this subject until Rockey's scholarly and comprehensive investigation in 1916. As a consequence of the light cast by this brilliant paper many cases were recognized and published; in most instances these articles have been brief and confined themselves to some particular phase of the condition.

The senior author, having met with the case of uterus didelphys described below, has felt it would be desirable to resurvey, after a passage of twenty years, the literature which has accumulated in the English, Spanish, German, and French journals.

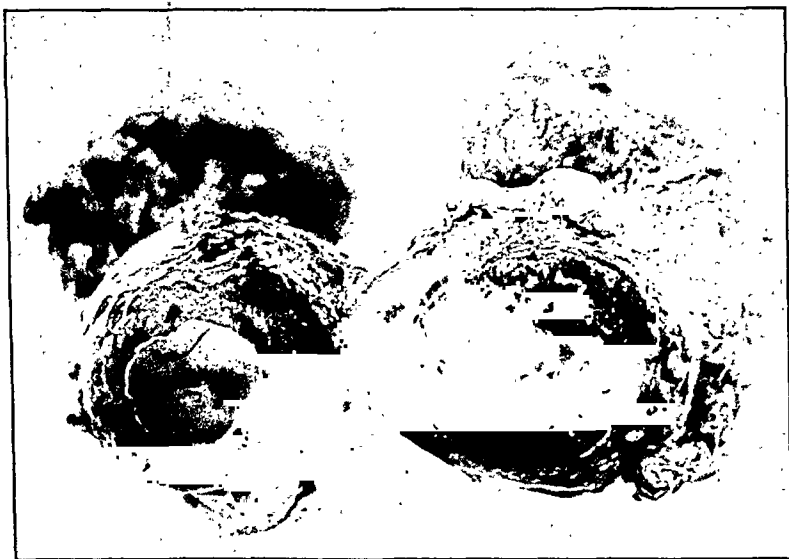


Fig. 1.

CASE HISTORY

Mrs. H. R. D., 27 years of age, presented herself, complaining of severe dysmenorrhea. She stated that menstruation began at the age of 13 and has always been irregular. The menses, six to seven days in duration, were very painful and accompanied by nausea and vomiting. There was an associated loss of weight which was usually regained shortly thereafter. A dilatation and curettage at 17 failed to relieve this complaint. At this time a diagnosis of double uterus with vaginal septum was made.

She was married at the age of 21 and conceived at 26, the pregnancy being marred by marked nausea, vomiting, and fainting spells and an umbilical hernia. At the eighth month a 5½ pound baby of perfect form was delivered. The patient contracted postpartal pneumonia, which almost cost her her life.

This means, as we have shown, columnar epithelial proliferation. It blocks the racemose glands, produces Nabothian cysts and, by hyperplasia, increases the alkaline downpouring from the cervix. The vagina cannot maintain its acidity with the overproduction from alkaline endocervical hyperplastic glands. Such a cervix in time may block sufficient number of the alkaline producing glands to cut out the excess alkaline downpouring permitting the vagina to pile up its acids without neutralizing them. Squamous epithelium will return to such a cervix, but too late to preserve a normal cervical structure, and the diseased gland-bearing mucosa of the cervix must be removed. In the following report the amount of organic vaginal acids produced from the desquamated vaginal epithelium by fermentation will be tabulated along with the vaginal pH and exact histological pictures of the cervix uteri.

I believe that vaginal pH is the primary factor in inducing these structural changes in the cervix uteri especially in nulliparous women and not infection per se, except as infection changes the vaginal pH. For in the mycosis fungi vaginitis cases (pH 3.0 to 4.0), I have yet to see columnar epithelium proliferation on the vaginal portion of the cervix as in all other acute vaginal infections when the pH is 6.0 to 7.5.

To further evaluate the effect of vaginal pH 6.5 to 7.0, apart from the effect of vaginal infections, antiseptics which do not in themselves stimulate or retard epithelial changes are now being added to the alkaline capsules.

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Sixty pregnant women with varicose veins were treated by the injection of quinine urethane with satisfactory results in 97 per cent. Although slight inflammatory reactions occurred, the relief obtained more than compensated for the previous discomfort. No serious complication resulted, and the puerperium was uncomplicated.

Of three patients who had subsequent pregnancies, only one had a slight recurrence of varicose veins. In Solomons' opinion, the injection of quinine urethane in 2 c.c. doses does not affect the pregnant uterus.

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in broadly built women of stable temperament. Ancel and Villemain (Puddicombe, 1929) attribute the malformation to the presence of a vascular fold, the vesicorectal fold, which is found only in the female and is almost constant according to Polak (1923) and Okinezye, Huet and Patocki when the bodies of the uterus are widely separated. This fold extends from the upper part of the rectum to the bladder and is produced by a branch of the superior hemorrhoidal artery. It was mentioned as present in 52 of 600 cases of double uterus by Dubreuil-Chambardel (1927-1928). It is referred to as having an allantoidal origin, or being caused by fetal peritonitis, or a relic of the terminal intestinal mesentery (Eden and Lockyer¹⁴); while conceded by many authors as an etiologic fact, Basset (1933) found five cases of double uterus in which no vesicorectal septum was present. Some authors, among them Nagel (Puddicombe, 1929), deem the fold the result of a double uterus.

Another theory is that the ducts of Mueller are held apart by an abnormally short round ligament. Newton (1924) refers to Pick who found tumors present in thirty cases and claimed that the presence of tumor had an etiological bearing. According to Felix and Rosenstein (Puddicombe, 1929) formative disturbances of the intestinal tract and developmental errors of the ventral abdominal wall are etiological factors. Keibel and Mall have collected from literature nine theories to account for these disturbances such as hydronephrosis, distention of bladder and rectum; anomalies in the formation of the abdominal wall such as hernia, cleft pelvis, etc., and fetal peritonitis. Like many other conditions uterine duplicity is probably due to a combination of causes.

Duplication of the uterus and vagina with its variations, one of the commonest of the congenital anomalies of the genital tract (Kussmaul, 1859), is seen comparatively infrequently. Stolper states that it occurs in 10 out of every 7,400 women, while Neugebauer places the frequency much lower at 3 in 19,000 (Findley, 1926).

Pregnancy and Double Uterus.—Fertility and frequency of conception in this condition are not particularly affected (N. F. Miller, 1922, and Polak, 1923) but successful termination of pregnancy is rare (C. K. Miller and Green, 1935). During pregnancy the nonpregnant half serves as an appendix to its mate, which on enlarging commonly drags the former posteriorly thereby frequently retarding labor by its incarceration in the hollow of the sacrum and by its hypertrophy (Granzow, 1932). The greater the uterine contraction the greater the resistance offered by the incarcerated half (Mueller, 1873, Borinski, 1876, and Holzapfel, 1893), which may also contract during labor and thus contribute to labor pains. In many cases the cervix of the nonpregnant half is found to dilate and commonly by the third, fourth or fifth day of the puerperium its decidua is cast off either entirely or in fragments. According to Cerqua, one horn may menstruate while pregnancy exists in the other (N. F. Miller).

In the minds of some (Findley, 1926) there seems to have been grave doubt as to the ability of the pregnant half to perform its function and an unwarranted emphasis has been placed on the casualties involved in labor. According to Strassman (1907) pregnancy in this uterus is as dangerous as an ectopic pregnancy and opinion varies as to the advisability of allowing such patients to go through a normal labor. Still, many do so with no untoward results. According to Abramson (1934) and Findley (1926) delivery in this condition should be by cesarean section to eliminate exhaustion of the patient by prolonged labor with undue complications. Bilateral, simultaneous pregnancies which are rare (Bernard, 1904, and Trapet, 1906) and seldom go to term have been described (Opitz, 1899, Satschawa, 1879, Pluemcke, 1927, Cramer [Salacz]).

There is a difference of opinion among obstetricians regarding the extent to which double uterus may complicate labor. Sweet (1934) and Guirin and Valmale (De Sa, 1928-1929) find that complications are less common than ordinarily supposed and many cases have been discovered by mere chance. Labor is usually prolonged because of weak deficient uterine musculature, which does not allow normal distention (Jung, 1927). Abortion is frequent, occurring in 21 to 28 per cent of cases (Giles, 1895, Miller, 1922, Findley, 1926, Dunning and Sanders, 1936), due either to abnormal implantation of ovum due to malformation or to the malformation itself. Uterine rupture is fairly common. According to Werth and Fehr (1917) 45 to 76 per cent

On examination, a year after this delivery, it was found that the head, neck, thorax, abdomen, and extremities presented nothing of note. Bimanual examination revealed a vaginal septum and laceration of the perineum and right cervix (Fig. 1) from the birth of the child. The left cervix was nulliparous. Bilateral cystic oophoritis was present.

Operative Procedure.—The right cervix and perineum were repaired. The abdomen was opened by a low midline incision, and bilateral endometriosis with marked adhesion to the surrounding structures were noted. These adhesions were freed, the double uterus dissected away and a supravaginal hysterectomy, a right oophorectomy, and an appendectomy were performed. The uterus was a typical double uterus with a single tube and ovary to each horn. The patient recovered and is now enjoying good health.

EMBRYOLOGY AND ETIOLOGY

The etiology of double uterus lies in some mechanical obstruction preventing complete union of the paired ducts of Müller. These ducts, indicated in the embryo of 10 mm., later may be divided into three parts, a cranial vertical portion, a horizontal portion, and a lower vertical portion, from which the uterine tube, the fundus and corpus uteri, and the cervix uteri and vagina are differentiated, respec-

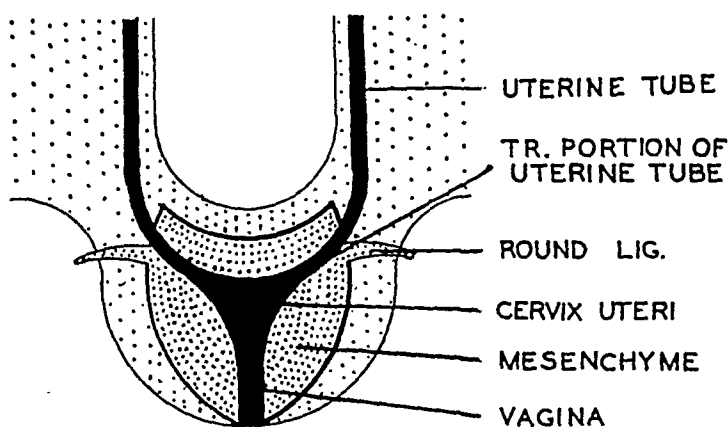


Fig. 2.

tively. At the medial end of the horizontal portion there is a union of the two urogenital folds, which contain in addition the excretory duct, to form the genital cord which the lower vertical portion of the Müllerian ducts traverse. Between the 22-28½ mm. stage there occurs a union of the right and left Müllerian ducts in the genital cord and the unpaired canal is termed the uterovaginal canal. Normally, the union takes place first in the second fourth, that is in the region of the cervix, and proceeds cranially to the upper end of the genital cord and caudally to some point in the vagina, the precise location of which is a subject of discussion. This union is at first an external one. Later the apposed walls fuse to form a septum which is resorbed in a caudal direction. From the uterovaginal canal the cervix, and at least a portion of the vagina, are differentiated (Fig. 2). By the bulging of the cranial wall of the horizontal portion of the Müllerian ducts with the concave junctional region of the two ducts becoming convex, the fundus and corpus uteri are formed, resulting in the unfused transverse (horizontal) portion of the ducts being added to the fundus and corpus of the uterus. Failure of the Müllerian ducts to fuse cranial to the original site of fusion (second fourth of the lower vertical portion) results in the duplication of the cervix and body of the uterus, while failure of absorption of the septum of the uterovaginal canal results in a double vagina.

Theories as to the origin of uterine duplication are varied. Eck (Sanders, 1936) believes that these malformations are due in some cases to some constitutional or germinal defects and finds that duplicity of the genital tract is most frequently found

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CHORIONEPITHELIOMA OF THE UTERINE TUBE

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CHORIONEPITHELIOMA arising from the chorionic epithelium of an ovum implanted in the uterine tube is an exceedingly rare condition. Very frequently it is not recognized at operation. Frozen sections taken during the procedure may not reveal the true nature of the growth. The following report shows the difficulty of making the true diagnosis even with roentgenologic and pathologic studies.

On Sept. 29, 1936 a twenty-nine-year-old white, married female entered Duke Hospital complaining of slight vaginal bleeding which had been noted for the previous seven days. Her last period had started July 20, 1936 and had lasted five days. Her previous period had started June 20, 1936 and had lasted twenty-one days. She had suffered from nothing more serious than vague lower abdominal discomfort and had had no symptoms suggestive of extra-uterine pregnancy. She had lost 14 pounds during the month prior to entry but complained of no pulmonary symptoms. For the week prior to entry she had suffered from morning nausea. Her menses had

of cases of rupture were in double uterus. According to Miller (1922) the complicating factors in abnormal deliveries at term in order of frequency are: 1, enlarged non gravid uterus; 2, vaginal septum; 3, uterine inertia; 4, tetanically contracted uterus; 5, retention complications; 6, eclampsia, which complications, excepting eclampsia, are usually due to maldevelopment of the uterine musculature (Iraeta and Hargundeguy, 1928). Less serious complications are very frequent (Rhemann, 1934).

In 11.9 per cent of Miller's cases third stage labor was complicated and required manual removal of the placenta due probably to malposition and interference with normal uterine contraction by the nonpregnant half of the uterus. However, complications do not stop with the third stage. Post-partum hemorrhage and subinvolution occur more frequently than normal. Free drainage of lochia may be prevented by malposition of the uterus due to its obstructing companion.

In the nonpregnant state menstruation may take place every two weeks, first on one side, then from the other, the patient losing in all about as much blood as during a normal period (Bainbridge, 1924). The possible complications of the nonpregnant uterus (Sweet, 1934) are dysmenorrhea and the so-called retention complications, hematocolpos, hematometra, and hematosalpinx, which are next in importance to the obstetric complications. These conditions result, if, in addition to the anomaly there is atresia of the vaginal or cervical openings. However, there is no evidence to show that these lesions are any more frequent in double uterus than in the normal organ. Other complications as dyspareunia and sterility are due usually to the vaginal septum.

Unless the possibility of the anomaly is borne in mind, there is a chance that its occurrence will lead to a mistake or difficulty in diagnosis (Catlin, 1928). Clinical recognition of the condition is of much importance because of its influence on the child-bearing function, and the diagnostic difficulties the uteri present when complicated by tumor formation, to which they seem prone (Dannreuther, 1927). The condition is of little clinical significance except in case of pregnancy, in which condition it carries the possibility of very serious maternal and fetal consequences (Sanders, 1936), although from a study of the literature one is impressed by the frequency with which this anomaly remains undiagnosed even in event of childbirth (Findley, 1926).

Diagnosis of this condition is presumably difficult, judging from the many instances in which the condition has failed to be recognized, being diagnosed as pregnancy complicated by fibroid, ovarian cysts, or as ectopic pregnancy. In differentiating the mass from ectopic pregnancies, Williams (1914) reminds us that the round ligament comes on the proximal part of mass in ectopic pregnancy while in uterus didelphys it comes off the distal portion. In most cases the diagnosis was not made until after a laparotomy revealed a double uterus. Unless there is a definite history of menstrual disturbances, delayed onset of menstruation or semimonthly bleeding the history is of little diagnostic value. Dysmenorrhea is suggestive; this occurs in about 20.3 per cent of these cases (N. F. Miller, 1922). A history of abdominal pain, since it occurs in other conditions is of little diagnostic value. In no case are the pains referable to doubling of the uterus (Werth and Fehr, 1917). Pain in double uterus is always suggestive of an associated retention complication. Menorrhagia and dyspareunia are incidental. Amenorrhea is rare. The average age of onset of menstruation is 15; beginning in some of these cases as late as 26 and in several cases being absent. Malformation of external genitalia should lead to suspicion. In some cases the vesicorectal fold could be palpated (N. F. Miller, 1922). According to Abramson (1934) cases in which there is question should be submitted to hysterosalpinagraphy, for which Cervato and Levine recommend lipidol.

Treatment in these cases varies considerably and should be conservative whenever possible. Surgical interference is rarely necessary and according to Sweet (1934) to recommend surgical measures in these women with no other justification than the mere presence of this anomaly cannot be justified on the basis of his experience and to operate except for some known pathologic condition is no more reasonable for them than it would be for a normal person.

thin pellicle surrounding old blood. The uterus was about one and a half times normal size and of smooth and regular contour. The left ovary contained a small corpus luteum and was of normal size. Both left tube and ovary were lightly

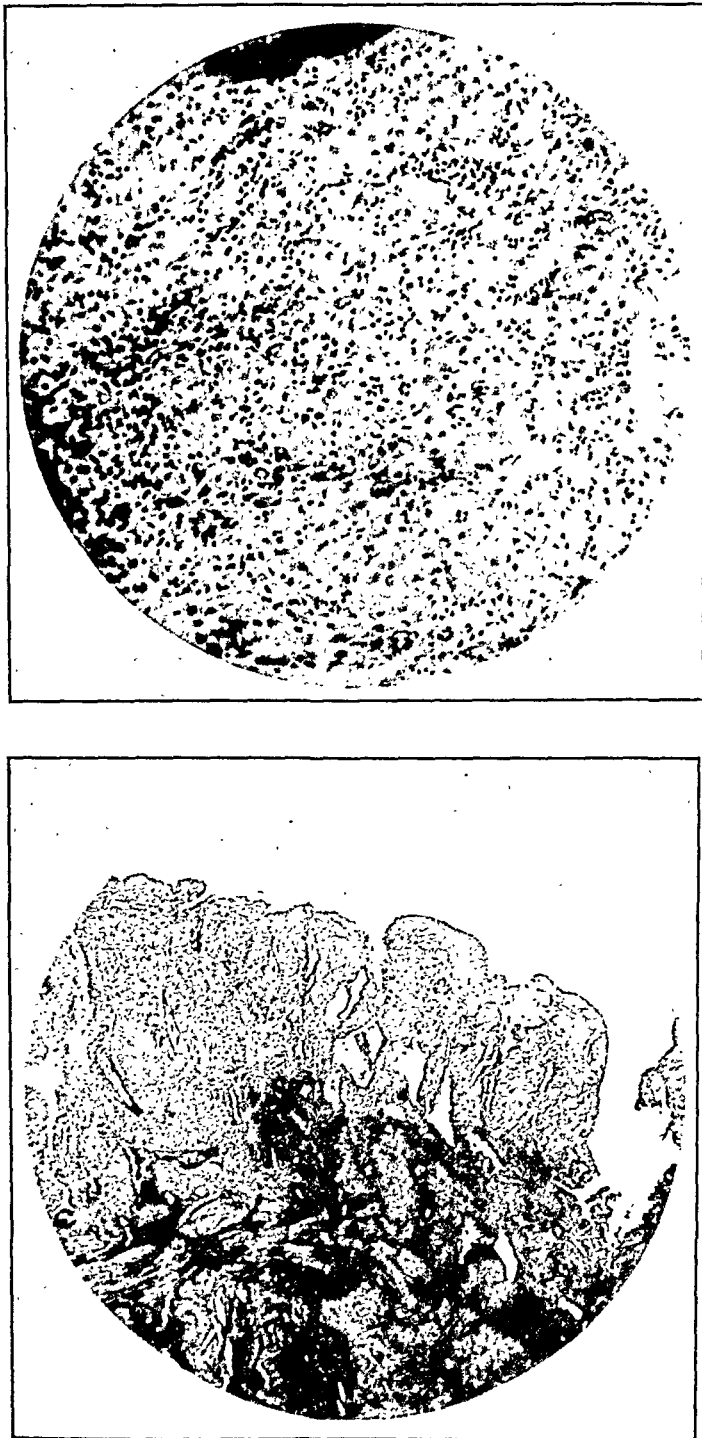


Fig. 2.—High and low-power photomicrographs of the decidual reaction in the uterus.

adherent to the posterior leaf of the broad ligament. The right adnexa were never identified but the uteropelvic ligament fortunately was not involved in the mass. A supravaginal hysterectomy with removal of adnexa was performed. The anterior wall of the rectum and cul-de-sac oozed considerably. Hot packs controlled this

occurred up to the present illness at intervals of twenty-eight to thirty days, and the periods had lasted about five days. During the year prior to entry her menstrual flow had become somewhat more profuse. She had had two normal pregnancies which terminated spontaneously at term, the first in 1928 and the last in 1929. Both children were living and well.

Physical examination revealed a thin, pallid, young white female in no obvious discomfort. Her temperature was 37°C ., pulse rate was 100, and respiratory rate was 20. Her blood pressure was 110/70. The heart and lungs were entirely negative. Nothing significant was found except in the abdomen and in the pelvis. There was a firm, slightly tender mass arising 10 cm. above the symphysis. The mass was a little higher on the right side and was fixed. Pelvic examination showed normal external genitalia. The perineum was slightly relaxed. The vagina was normal and no masses were found in it. The cervix was blue, soft, slightly lacerated, and was continuous with the abdominal mass. The mass was firm on the left side and on the right side was globular, suggestive of a pregnant uterus.

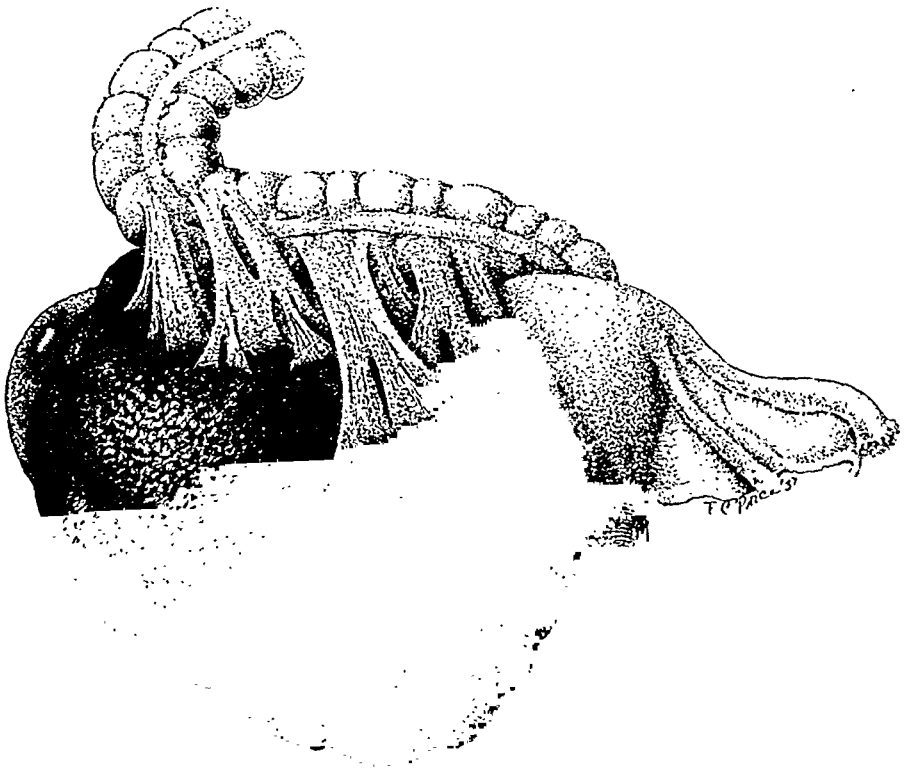


Fig. 1.—Diagram of the findings at operation.

The accessory clinical findings were hemoglobin 82 per cent (Sahli), red cell count 4,080,000, white cell count 11,800, differential normal, urine negative, and sedimentation rate of 10 mm. in thirty minutes.

Because of the weight loss and lassitude a "chest plate" was taken. The report was "Examination of the chest shows the lung fields to be essentially clear, except for slight increase of the hilar shadows and bronchovesicular markings." The basal metabolic rate was +9 per cent.

The diagnosis of pregnancy complicated by fibromyoma was made and hysterectomy was advised. On the ward the patient continued to have a slight continuous uterine discharge of what appeared to be old blood. She also had a tachycardia which at times was as high as 100 on absolute bed rest.

On Oct. 3, 1936 coeliotomy was performed. A midline suprapubic incision was made. The omentum was found to be adherent to a nodular, dark colored mass about 12 cm. in diameter arising from the adnexal region. The rectum and sigmoid were adherent across the top of the mass. The adhesions were freed. In attempting to lift the mass from the pelvis it broke open and was found to consist of a

M. Krusei: The growth of these organisms was characterized by the irregularity in size and shape of colonies which appeared to be equally well isolated. There were variations in size (0.2 to 1.0 mm. in diameter), the surface appeared flat, ridged or nodular, and the edges of different colonies were smooth and round or coarsely irregular.

M. stellatoidea: This organism, which resembled *M. albicans* very closely on Sabouraud's dextrose agar, presented a very characteristic appearance on blood agar. The surface was heaped up in the center and from this center zone "arms" radiated in an irregular fashion. These projections were thick near the center and narrowed at the periphery, giving the colony an appearance not unlike that of a "star in the sky" with its surrounding radiations of light (Fig. 2).

Cryptococcus sp.: All strains of this fungus grew very poorly on blood agar and never attained any appreciable size.

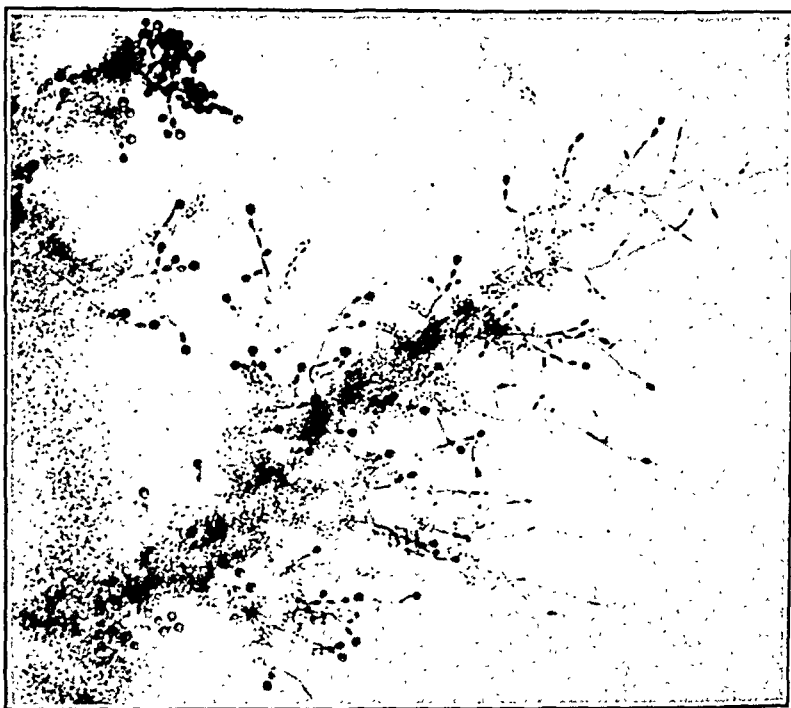


Fig. 3.—Photomicrograph of corn meal agar slide culture of *M. albicans* fixed and stained with lactophenol cotton blue.

Mycelial Development on Corn Meal Agar (Several Days at Room Temperature).—Constant results on this medium were obtained only if the inoculum had been on the sugar free medium (beef extract agar) for several generations. Different strains of the same species showed variations in mycelial development but certain "typical" structures were usually present. The following descriptions are confined to the most constant features found in each species.

Monilia albicans usually produced a well-developed branched "tree-like" mycelium which did or did not extend far from the original streak. The most constant finding was the development of numerous swollen double contoured cells (chlamydospores) on the tips of most all branches (Fig. 3).

M. parapsilosis: The mycelium seemed to form much less readily than in any other species, but after development occurred branching was profuse. There were no chlamydospores.

oozing. The abdomen was closed with 2 rubber protective drains in the cul-de-sac. The nature of the lesion was never exactly determined in the course of the operation but was considered to be either endometriosis or an extra-uterine pregnancy.



Fig. 3.—High and lower power photomicrographs of the neoplasm. The syncytial elements are clearly visible.

The patient had a tachycardia of 140 for the first three days following operation and her pulse was then from 80 to 100 for the rest of her stay. The first day after operation she was given a transfusion of 450 c.c. of citrated blood although her hemoglobin, red blood count and blood pressure were satisfactory. There was no

evidence of internal bleeding, and forty-eight hours after the operation the drains were removed. Her subsequent postoperative course was uneventful. Nothing was ever demonstrated in her chest. The wound healed well. She was discharged on the thirteenth postoperative day. Her pelvis showed no induration on discharge, and no masses were observed in her vagina.

The pathologic report was: "Ectopic pregnancy. Decidual reaction in uterus and right tube." The specimen consisted of a uterus, both tubes, and both ovaries. The uterus was 4.5 by 6.5 by 7.5 cm. The cavity was smooth and the endometrium was 4.0 mm. in thickness. The left tube and ovary were normal in appearance except for a few shaggy adhesions on their surfaces. There was a small corpus luteum in the left ovary. The right tube, ovary, and lateral wall of the uterus were involved in a carneous mass about 12 cm. in diameter. The right ovary was cystic and had a sac 4 cm. in diameter with a fibrous lining. The sac was buried in the inferior lateral portion of the carneous mass. Remnants of the right tube were

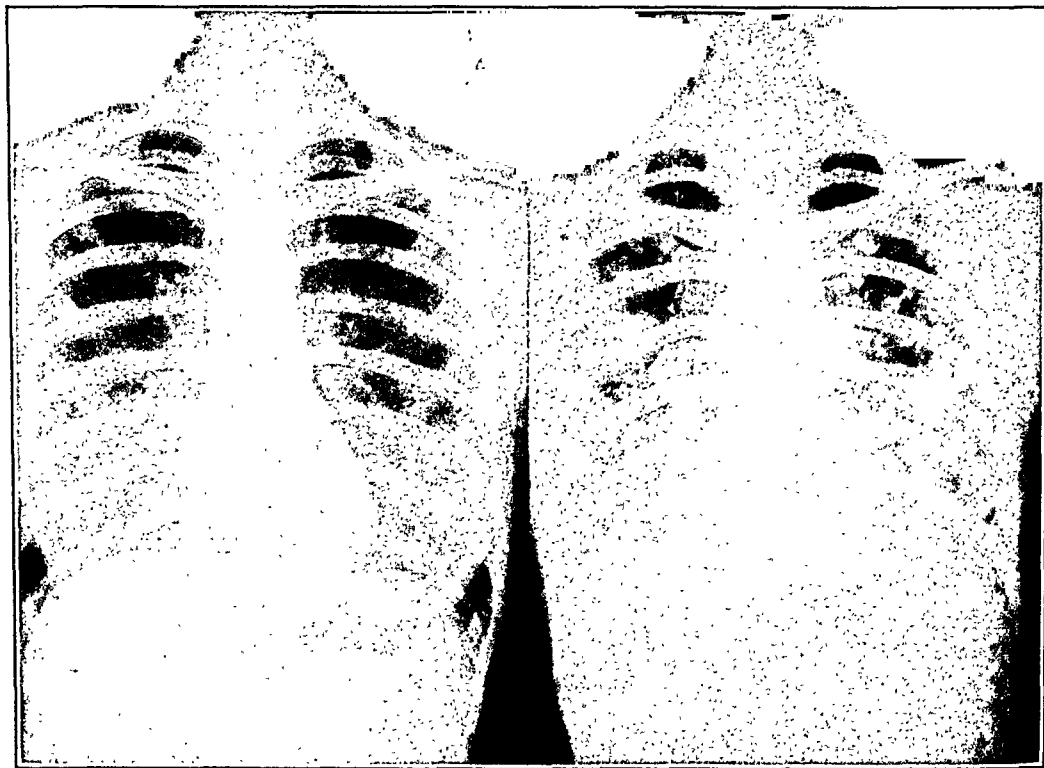


Fig. 4.—X-ray plates of the chest taken September 30, and November 4. Metastases are visible in the first plate in the lower right lobe, and in the second plate as rounded, discrete tumor nodules throughout both lungs, especially at both bases.

apparent on the surface of the mass. Sections were taken of the endometrium, both ovaries and left tube and of the mass. The endometrium showed a marked decidual reaction. Both ovaries and the left tube showed nothing significant. "The mass contained chorionic villi and decidual cells."

She entered the hospital again on Nov. 4, 1936. On Oct. 29, 1936 she had suddenly developed a pain in her left chest and dyspnea. She had no cough or hemoptyses. Her local doctor was called and told her that her "heart was beating too fast." Two days later, she developed pain in her left shoulder. Physical examination showed a temperature of 37.7° C., pulse of 140, and respirations of 40. She had lost weight but was in no distress. The left side of her chest was fixed. Her heart was of normal size; the rhythm was regular. There were no murmurs and the mediastinum was not displaced. The left lung was dull at the base and medium râles were audible throughout it. The right lung showed nothing remarkable. Hemoglobin was 76 per cent (Sahli), red cell count 3,830,000, and the white cell count 11,760. The catheterized urine specimen was negative except for a few white cells. Sedimentation rate was 28 mm. in thirty minutes.

X-rays of the chest showed rounded, discrete tumor nodules extending throughout both lungs especially at both bases. Examination of the abdomen and pelvis was negative and there were no tumors in her vagina. The operative scar was well healed.

The pathologic sections were reviewed and new ones were cut. The lesion in the right adnexal region was found to be exceedingly anaplastic and the correct diagnosis of chorionepithelioma was made. Subsequent examination of the chest plate made on her first admission showed two areas of increased density that undoubtedly represented early metastases. A quantitative Zondek-Aschheim test showed 100,000 to 500,000 rat units of gonadotropic hormone per liter of urine.

A hopeless prognosis was given. The patient was given 1,000 roentgen units of teleroentgen therapy over her entire chest and abdomen from Nov. 9 to 19, 1936. She developed a leucopenia, of 3,000 white cells, and her condition grew worse. She was given 450 c.c. of citrated blood on November 20. She was very anxious to be with her family and was allowed to return home on Nov. 22, 1936. It has subsequently been reported that she died. Unfortunately no autopsy was performed.

The presence of metastases to the lungs was not recognized at the time of her first entry, and the lesion was not correctly diagnosed at the time of operation or after microscopic examination of the tissue. Had total hysterectomy with bilateral salpingo-oophorectomy been performed and had roentgen therapy started immediately after operation, the outcome might have been different. Irradiation was started when the patient was in a hopeless condition. Because of the rarity of the lesion others have had difficulty in making the correct diagnosis. Philipp¹² has reported a case of chorionepithelioma occurring in the right broad ligament. The patient had had dilatation and curettage about six months prior to operation. At the time of operation it was felt that the lesion was probably an old blood clot resulting from trauma to the cervical artery. A frozen section showed only old blood. The right ureter passed through the mass. The diagnosis of chorionepithelioma was made upon subsequent examination of the tissue removed.

Chorionepithelioma of the uterine tube was first described by Sanger and Marchand from 1888 to 1895.⁹ According to Fleurent⁹ and others, 32 cases have been described up to 1933. Thomas¹⁰ and Motta¹¹ have reported 2 cases subsequently. This brings the total number of reported cases to 35, including the present case, and not including Philipp's case in which the tumor was not in the tube but in the broad ligament. Jeanneret⁹ in reviewing a series of 350 cases of chorionepithelioma found 11 primary cases in the tube, an incidence of 3.14 per cent. At the Free Hospital for Women, Brookline, Massachusetts, one case of chorionepithelioma was encountered between 1900 and 1925. At Duke Hospital two patients with chorionepithelioma including the present have been operated upon since 1931.

The reports of most cases in general have been similar. The patients have complained of symptoms of and presented the findings of an ectopic pregnancy. The patients have usually undergone operation. Following either a radical or a conservative procedure a latent period of several months has ensued, and then the patient has reappeared with her lungs and brain riddled with metastases or with a huge lower abdominal mass. Most patients in the beginning complained of lower abdominal pain and irregular bleeding. (Risell, Phillips, Cope and Kettle, Hartz, Solomons, Duggan, Fleurent, Thomas and Motta.) Most patients have presented an unilateral adnexal mass on vaginal examination. Vaginal metastases associated with chorionepithelioma of the tube have been reported by Phillips,² Solomons,⁷ Duggan,⁸ and Motta.¹¹ These vaginal metastases have had the appearance of those associated with chorionepithelioma of the uterus and have been described as being rounded, plum colored, and occasionally ulcerated.

Miles Phillips² in 1911 reported a case of chorionepithelioma of the tube in which a remarkable recovery occurred. The patient had a salpingectomy performed for a tubal gestation. The pathologic report was chorionepithelioma. The uterus was curetted and no decidua or tumor was found. The patient then developed a recurrence in the broad ligament. A total hysterectomy was performed, and a malignant nodule excised from the bladder and vagina. A large nodule in

the root of the mesentery was inoperable. The patient was living and well four months after the last operation and the mesenteric nodule had diminished considerably in size. Hartz's⁶ patient was living and well two years after right salpingo-oophorectomy. Philipp's¹² patient, although a case of chorionepithelioma of the broad ligament, showed a negative Zondek-Aschheim test twelve days after hysterectomy and excision of the tumor mass in the broad ligament. Fleurent⁹ also mentioned two other cases of apparent recovery reported by Klein and Albert. Klein's patient had a chorionepithelioma of the right tube with metastases to the vagina and lung. Salpingectomy was performed and roentgen therapy was administered. In Albert's patient regression occurred after partial removal of the tube and tumor mass. Chorionepithelioma of the tube occasionally undergoes the remarkable regressions reported to occur in chorionepithelioma of the uterus. The prognosis cannot be considered hopeless.

Once the diagnosis can be accurately established, which seems to present the greatest difficulty in determining therapy, it would appear logical to perform panhysterectomy with bilateral salpingo-oophorectomy. The channels by which the neoplasm can metastasize to the vagina from the tube must be through the uterine cavity. It would also seem logical to administer a heavy series of x-radiation to the pelvis as soon as possible after operation because of the known radiosensitivity of chorionepithelioma. Fleurent's and Klein's patients received x-ray postoperatively. The former's patient died of recurrence and metastases, and the latter's patient recovered. These are apparently the only two patients to receive therapy immediately after operation. Thomas administered x-ray therapy to his patient only after large metastases to the bladder and culdesac had appeared, and it was apparently no more effective than in the case of the patient reported in this article.

SUMMARY

1. Cases of chorionepithelioma of the tube are exceedingly rare and difficult to diagnose. Thirty-five cases have been reported up to the present.

2. Most patients have presented symptoms and findings of an ectopic pregnancy. Following operation a latent period has ensued then recurrence or metastases have occurred.

3. Four cases of remarkable regression and recovery following chorionepithelioma of the tube have been reported.

4. Logical treatment for chorionepithelioma of the tube would appear to be panhysterectomy with bilateral salpingo-oophorectomy followed as soon as possible by x-ray in massive doses.

The authors thank Drs. Bayard Carter and E. C. Hamblen for permission to publish the above case.

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THE FORMATION OF AN ARTIFICIAL VAGINA WITHOUT OPERATION

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ABSENCE of vagina, as a rule associated with rudimentary solid uterus, is a not infrequent malformation. I have seen more than 30 cases in the last twelve years. The condition rarely is discovered before the patient has passed the age of puberty, at which time, at fifteen or sixteen years, the nonappearance of menstruation leads to a pelvic examination. These individuals, with few exceptions, are fully feminine. The vulva appears normal. The hymen is present but no vaginal opening can be found. Rectal examination discloses, particularly if a metal catheter is inserted into the urethra and bladder, a thin connective tissue plane separating urethra and rectum. High up a narrow strand represents the rudimentary uterus. If the abdominal walls are relaxed, small gonads can be felt at the site of the ovaries.

Some patients, when advised of their condition, react with severe mental depression, their entire outlook on life is changed, suicidal ideas may develop. Properly selected cases should be relieved. The most favorable time for establishing a vagina is when marriage and sex relations are contemplated in the near future.

Three main types of operation have been used in the past. The first utilizes the intestinal tract: small intestine, Baldwin operation; rectum, Schubert operation. I have never performed these as the risk is disproportionately great, the mortality of the reported and unreported cases being estimated at 20 per cent. The second type of operation of which the Graves' is an example, utilizes the mucous membrane of the labia minora for forming a mucous membrane lined canal. The third of which the Frank-Geist and Grad modification are examples, utilize pedicle flaps obtained from the inner side of the thighs. Recently free skin grafts (Wolff or Thiersch) have again been tried with favorable report of the results.

During the operations for formation of an artificial vagina, as well as in the examination of patients when first observed, I have been struck by the very tenuous tissues separating rectum from urethra and bladder. An incision in the hymeneal region gives ready access to this connective tissue layer and with a few penetrating movements of the fingers, the peritoneal fold of Douglas is readily reached. Motivated by this observation, in the last three and one-half years I have attempted gradually to force inward the mucous membrane in the introital region without incision or operation. By this simple maneuver, a vagina may readily be established without operative intervention. Six patients have now been treated, with only one failure, which is ascribable largely to the uncooperative attitude as well as

the stupidity of this patient. The establishment of the artificial canal is facilitated and its adequacy and permanence assured if the following procedure is followed.

PROCEDURE

The first object is to establish a narrow canal at least 2½ inches long as quickly as possible. After this depth has been attained, enlargement of the canal follows. The first step is important. A narrow pyrex tube, 0.8 cm. (5/16 inch) in outside diameter, is introduced by the physician in the center of the hymeneal region, in a direction backward and inward, with the patient in the lithotomy position (Figs. 1 and 2). The patient is carefully taught to perform this maneuver 3 times daily for at least a half hour for one week. This is important in order to stretch

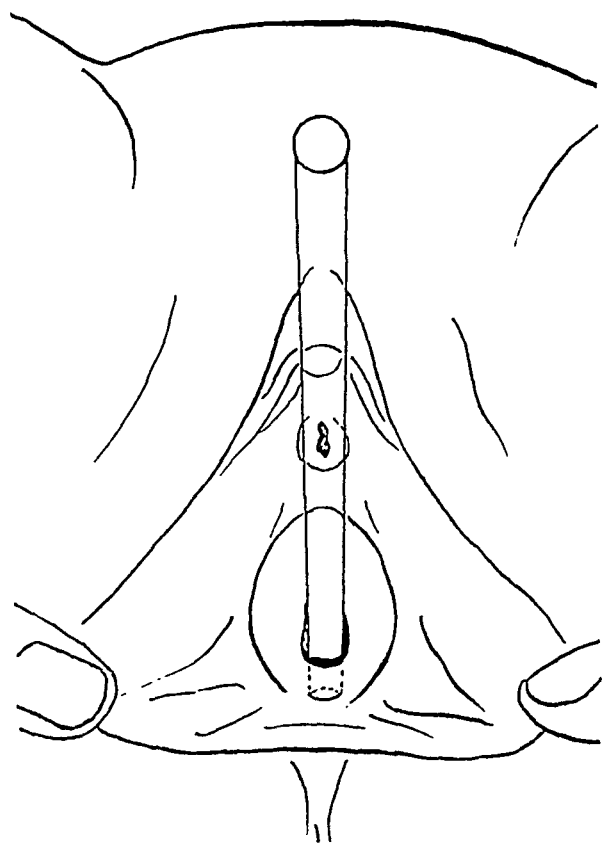


Fig. 1.—Labia separated. One-half centimeter tube introduced downward and inward to form pocket.

the mucosa so that further measures do not distort and dilate the urinary meatus. After the first week, the patient is taught to insert the tube downward and inward as before, but when this position has been attained, to change the direction of insertion in a line paralleling the normal axis of the vagina. (Fig. 2, 2). The tube is held in place for one-half hour in the morning, one-half hour in the evening. Usually in two to four weeks a sufficient depression permitting the retention of a 3 inch long tube has been attained. The shorter tube, as soon as it can be introduced for its full length, is kept in place throughout the night by a small pad of cotton and appropriate T binder. Within six to eight weeks, the full length of the vagina, 2½ to 2¾ inches has been reached. The patients are warned not to apply excessive force which manifests itself by spotting which indicates injury of the delicate mucosa lining.

It is now time to use a tube 1.5 cm. ($\frac{5}{8}$ inch) in diameter, inserted for the length of 7 cm. and kept in place every night for eight to ten hours. When this size tube is readily admitted, the final size, 2 cm. ($\frac{3}{4}$ inch) is used until marriage. In the earlier cases, still larger tubes were used but appear unnecessary. The 3 patients who have intercourse regularly, state that this is entirely satisfactory and normal, as do their husbands. Two patients are unmarried. In every instance I urge that the fiancé be fully informed of the situation in order that no unhappiness or legal repercussions may arise. The patients have thanked me warmly for having insisted on this, and they are now happily mated. The sole exception was the unintelligent patient, already married when first seen, who has sedulously kept her husband in ignorance and in whom the entire procedure has proved a failure. The 2 unmar-

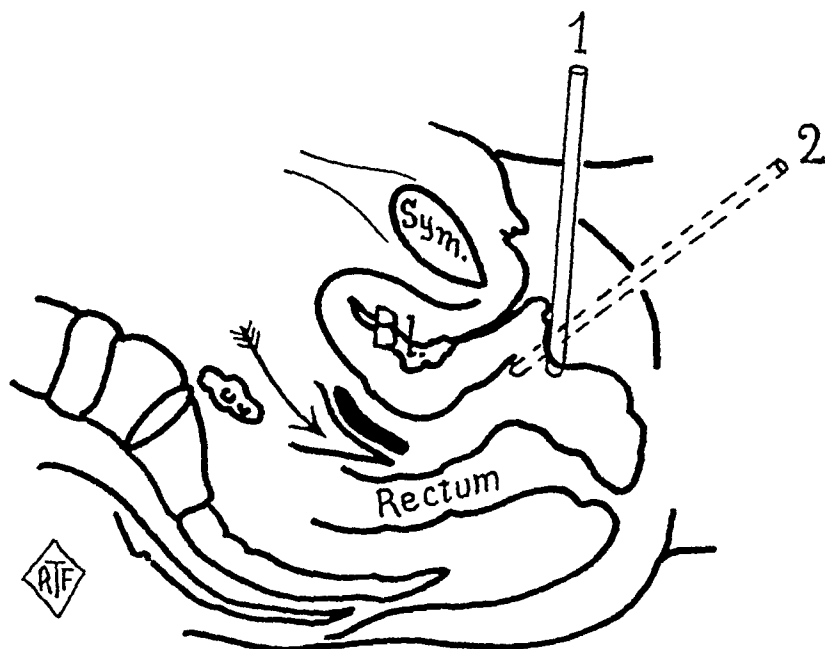


Fig. 2.—Schematic cross section of pelvis showing (1) tube introduced into first position; (2) more horizontal introduction after pocket has been formed. Arrow indicates the posterior peritoneal pouch of Douglas. In front of this is the small solid rudimentary uterus.

ried girls keep the tube in place every other night. Examination of all these patients shows a normal vulva and introitus. The vagina readily admits 2 fingers to the depth of $6\frac{1}{2}$ to 7 cm. ($2\frac{1}{2}$ to $2\frac{3}{4}$ inches) from the fourchette. The canal is lined with soft, resilient mucous membrane and a standard virginal speculum can be introduced and opened without discomfort to the patient.

COMPLETED CASES

CASE	AGE	MARRIED	LENGTH OF VAGINA	COITUS
U. N.	20	$3\frac{1}{2}$ years	7.0 cm. ($2\frac{3}{4}$ in.)	2-5 weekly
E. W.	19	$3\frac{1}{2}$ years	6.5 cm. ($2\frac{1}{2}$ in.)	1 weekly
L. R.	24	3 months	7.0 cm. ($2\frac{3}{4}$ in.)	2-6 weekly
S. G.*	22	3 years	7.0 cm. ($2\frac{3}{4}$ in.)	Rare
A. H.	$18\frac{1}{2}$	Unmarried	6.5 cm. ($2\frac{1}{2}$ in.)	-
L. K.	$18\frac{1}{2}$	Unmarried	6.8 cm. ($2\frac{5}{8}$ in.)	-

*Failure

It is hoped that with this bloodless and simple procedure, patients suffering from this malformation may be readily relieved of their coital disability and of the feeling of inferiority which this engenders.

PREGNANCY COMPLICATED BY GONOCOCCIC SALPINGITIS

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GONOCOCCAL infections in women extend to the tubes in from 15 to 30 per cent of the cases. These adnexal invasions occur most often just before, at the time of, or at the completion of menstruation. The gonococci in their upward dissemination are presumed by some authorities to pass over the fundal endometrium, which is rich in glandular tissue and highly suitable for their growth, and attack the mucosa of the tubes and there set up an inflammation.

Graves in his *Gynecology*¹ states that "the gonococci ascend and go through the internal os and directly attack the tubes, doing very little damage to the intervening endometrium which is used more or less as a bridge than a soil for permanent propagation." Curtis² in his *Textbook on Gynecology* states: "Extension of the infection is by way of the mucosa in contradistinction to progress through the wall of the uterus such as characterizes puerperal infection," and further that "The exact mechanism of invasion has not been demonstrated." Curtis has pointed out the frequency of so-called violin string or multiple band adhesions between the anterior abdominal wall and the anterior surface of the liver which are observed in abdominal sections on patients that have had gonococcal salpingitis. How does the gonococcus reach the capsule of the liver and the peritoneum lining the anterior abdominal wall? Surely not by surface extension. In these instances the organisms are either blood or lymph borne. Gilliam³ states that "Gonococcic infection of the endometrium is spoken of as specific endometritis. It constitutes a large proportion of the cases that fall under observation. In its unmixed form it is usually sub-acute. *The gonococcus seldom produces an acute inflammation in any situation.*" He also points out that infection of the tubes by the gonococcus almost invariably proceeds from the uterine cavity by continuity of the mucous membrane, but he adds that "gonococci may follow the blood and lymph channels." Evidences of his last statement are numerous and explainable on no other basis. Rubin⁴ in his monograph on gynecology makes the statement that gonococci are spread upward through the endometrial mucosa or through the lymphatics. A number of authors have taken the stand that the gonococcus is a "surface rider," but we observe many women of different ages suffering from specific salpingitis and are genuinely disturbed at the celerity of pelvic extensions. In a number of instances within forty-eight or seventy-two hours after exposure the infection has extended to the pelvic organs. Such rapid spread of the process we think is more an evidence of blood or lymph stream dissemination than surface extension.

In any large venereal disease clinic patients are seen with arthritis, lymphangitis, inguinal adenopathy and metastatic ophthalmia. We have found a sufficient number with a frank arthritis in which the contact is suffering from the same complication, to consider that there is conceivably a special strain of the gonococcus which has a predilection for the tissues of the joints. We have also observed that when one sexual partner has a severe complication in all probability the other will have a stormy recovery. This is especially true in blondes of either sex and has been pointed out by other writers.

CASE REPORT

White adult female, No. 40192, 24 years of age, married, occupation housework, admitted Jan. 4, 1937. Chief complaints: Pain throughout the lower abdomen with nausea and vomiting at times and profuse vaginal discharge. Was married at the age of 17, has had two children, aged 6 years and 8 months, both living and well. Has had several induced abortions. She uses beer in moderation, smokes excessively,

and is constipated. Menses began at 14 years, 28-day type, flow four to ten days, slight pains before and during the period. Last menstrual period Oct. 11, 1936. She had had an uncomplicated gonococcal infection in 1932 and since then she has had several interrupted pregnancies and a full-term baby. The baby is now eight months old. She stated that for the past three months her husband has been away at a CCC camp, and upon his return home he complained of a discharge and was found to be suffering from an acute gonococcic urethritis. The patient admitted having intercourse with him several times since his return.

A general physical survey disclosed a fairly well-nourished and well-developed female who did not appear to be acutely ill. Temperature 98.3° F., pulse 84. The skin and mucous membranes were clear. The heart and lungs were normal. Over the entire lower abdomen there were pain and discomfort on pressure. The vaginal examination revealed an acute urethritis, and purulent material could be expressed from the orifice. The cervix was hypertrophied, soft, cyanotic and covered with a mucopurulent discharge. The fundus was in a posterior position, soft and enlarged to about the tenth to the twelfth week of pregnancy. The right tube was greatly enlarged, tortuous and very tender. The left adnexa was apparently normal. Slides from the cervical secretion showed many typical intracellular diplococci.

We advised complete bed rest. This was carried out and after ten days the pain and discomfort were entirely relieved. Upon her return to the clinic she received subcutaneous injections of a foreign protein and at the end of three weeks local treatment was instituted. A bimanual examination was made at this time and the tube had diminished to half its size and was almost painless to pressure. She was making excellent progress under treatment but became delinquent. Through our social service follow-up we learned that she had applied to another clinic for continuation of her medical care. We have received discouraging reports of her progress and our informant stated that despite careful treatment the cervical and urethral slides remained positive for many months.

The patient was delivered at the Cook County Hospital on July 12, 1937, of a full-term normal female baby. Following delivery she had a recurrence of her pelvic symptoms and both tubes became involved. She was discharged from the hospital at the end of the third week. She is under treatment at a clinic at this time for her salpingitis. The patient's two children were examined recently and both were found to be infected. They are receiving treatment.

The exact mechanism of pelvic extensions in gonococcal infections has not been demonstrated but conceivably a specific infection with a complicating salpingitis during pregnancy precludes surface extension.

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TWIN ECTOPIC PREGNANCY*

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AREY in 1923 reviewed all reported cases of unilateral twin ectopic pregnancy. At this time, he was able to find 40 authentic cases including two of his own. In addition, he found 8 probable and 4 possible but doubtful cases.

We have been able to find reports of 23 additional authentic cases published since Arey's compilation. Two additional reported cases must be classed as doubtful. We wish to present 2 cases of unilateral twin ectopic pregnancy observed at Harlem Hospital, bringing the total number of reported authentic cases up to 65.

H. E. Jordan, and R. H. Meade, Jr., 1928. Twenty-two-year-old gravida i, para 0. Spontaneous abortion, one and one-half years ago. Last menstrual period seven weeks before operation; abdominal pain four weeks later. Laparotomy showed right monochorial twin tubal pregnancy. One twin was 7 mm. long; the other 4 mm., estimated to be thirty and thirty-six days old, respectively.

R. Brown, 1928, reports left tubal abortion with two fetuses lying free in the abdominal cavity, about two months old.

J. B. Dawson, 1928. Twenty-nine years old, para iii. Two months' amenorrhea. Six weeks after last menstrual period had lower abdominal pain and vaginal bleeding and was considered incomplete abortion. Two weeks later had sudden pain and operation revealed ruptured uniovular right twin pregnancy, estimated to be six weeks old.

S. P. Garrison, 1932. Multipara, 35 years old with a history of a ten-year sterility. Amenorrhea for eight weeks. Slight vaginal bleeding in the sixth week. Abdominal pain five days later. Mass felt eight weeks after onset of amenorrhea. Operation disclosed ruptured right monochorial twin ectopic pregnancy.

W. A. Jewett, 1933. Case of right unruptured twin ectopic pregnancy. Summarizes 9 other authentic cases which are accordingly omitted from further discussion here.

V. Finderle, 1933. Thirty-three-year-old, para i. Sterile period twelve years. Ten weeks' amenorrhea. Sudden onset of vaginal bleeding and pain. Operation showed ruptured left twin ectopic pregnancy; two fetuses, each 4 cm. long with separate umbilical cords which fused in the lower third.

P. Esau, 1934. Thirty-five-year-old, gravida ix, para vii. Last menstrual period seven weeks ago. Onset of abdominal pain and no bleeding. Operation revealed right ovarian cyst and right tubal twin pregnancy and left dermoid cyst.

K. De Snoo, 1934. Twenty-eight-year-old woman. Amenorrhea for seven months. At this time, abdominal pain and vaginal bleeding occurred, simulating premature labor. It was concluded that the pregnancy was extrauterine and laparotomy performed. An intraligamentous twin pregnancy was found; the fetuses were macerated and weighed 2,010 gm. and 1,500 gm., respectively. There was only one amnion present.

K. Podleschka, 1934. Three months' amenorrhea with sudden severe pain and vaginal bleeding. Two fetuses apparently uniovular, 10 cm. and 6.5 cm. long were found. The larger appeared normal and the smaller abnormal.

C. B. Lull, and J. B. Bernstein, 1934. Thirty-five-year-old woman, with history of last menstrual period five months before operation. In the fifth week of amenorrhea a catheter was inserted into the uterus. Eleven days later, vaginal bleeding occurred. This was considered to be an incomplete abortion.

*Presented at a meeting of the section on Obstetrics and Gynecology of the New York Academy of Medicine, October 26, 1937.

M. candida: The mycelium developed readily and extended far from the line of streak. The main mycelial threads grew in straight parallel rows and the lateral branches were shorter than those of *M. albicans*. There were no chlamydospores.

M. Krusei produced mycelia which, when well developed, showed long branches occurring at rare intervals. Clusters of long thin spores were found arranged like a bundle of crossed sticks.

M. stellatoidea formed mycelia readily and was characterized by large numbers of large balllike clusters. These developed on the mycelial strands and grew so closely together that the mycelial threads connecting the clusters were difficult to see. A single chlamydospore was found in 2 of the 29 strains studied (Fig. 4).

Cryptococcus sp.: No mycelium developed in any of the 9 strains studied.

Fermentation of Carbohydrates (14 Days at 37° C.).—Constant carbohydrate fermentations were obtained only after the inoculum had been kept on sugar-free medium for 2 or 3 transplants and when the tubes containing the carbohydrate broth were sealed with vaseline. The following 9 carbohydrates were tested with all



Fig. 4.—Photomicrograph of corn meal agar slide culture of *M. stellatoidea* fixed and stained with lactophenol cotton blue.

strains: dextrose, saccharose, lactose, maltose, levulose, dextrine, galactose, mannite, and inulin. Slight variations in fermentation occurred with some species if the original broth was not titrated to pH 7.2. The ability of each strain to clot milk was tested by the method described by Stovall and Bubolz.³ Table I lists the fermentations obtained with the various organisms and our results indicate that only the first four sugars need be used. Three organisms, *M. parapsilosis*, *M. Krusei*, and *cryptococcus* ferment the same sugars, but can be differentiated easily by the other criteria already mentioned.

Ascospore formation: All strains were kept on carrot plugs at room temperature for 60 days before discarding. Smears were made at frequent intervals and examined for asci. None was found in any of the cultures.

Agglutination tests: Numerous agglutination tests were done on most of the strains studied, with various modifications of Benham's² technique, and our results agree with those obtained by her. Except for *M. albicans* and *M. candida*, which appeared to be identical antigenically, the other species showed certain antigenic

CASE 2.—M. D., a 34-year-old gravida iii, para iii, colored woman was admitted to Harlem Hospital on Nov. 17, 1932. Her last delivery had been six years ago. Her last normal period had been four months previous to admission. The following month she missed her period but in the next month began to have vaginal spotting. Six weeks before entry, she went to bed because of vomiting and fainting spells. While in bed, the vaginal bleeding stopped until eleven days before admission when she began to have severe abdominal pain, associated with recurrence of bleeding.

Abdominal examination revealed a mass extending four fingers above the symphysis. Vaginal examination showed the cervix to be soft and patulous. Moderate vaginal bleeding was present. The uterus at this time appeared to be irregularly enlarged; no adnexal masses were felt. No fetal heart sounds were heard. At this time she was considered to have had an incomplete abortion with



Fig. 1.

possible fibroid uterus. The blood count except for moderate anemia was normal. Sedimentation rate was normal. X-ray of the abdomen showed no evidence of fetal parts. The Aschheim-Zondek test was negative. The patient was observed for one month during which time the abdominal mass remained unchanged in size. A low grade temperature which was present on admission gradually subsided. Vaginally a globular mass became more distinct in the right fornix. This mass was believed to be a dermoid cyst of the ovary rather than an ectopic pregnancy. At laparotomy, considerable difficulty was found in entering the peritoneum due to a mass which was densely adherent to the parietal peritoneum and adjacent omentum and intestines. It was thought that this mass had its origin in the right tube but no normal anatomy could be demonstrated. The mass was excised and the abdomen closed without drainage. Convalescence was uneventful and the patient was discharged thirteen days after the operation.

Five months after her last menstrual period, she had severe abdominal pain and x-ray at this time showed evidence of twins. Laparotomy disclosed a twin abdominal pregnancy with no microscopic evidence of adnexal or uterine tear. The fetuses are not described.

McGregor, 1934. Thirty-five-year-old woman with secondary abdominal pregnancy; single placenta with one full-term fetus and one macerated fetus was found free in the abdominal cavity. Full-term fetus died within one hour.

J. A. Ferguson, and I. S. Otis, 1935. Thirty-two-year-old woman, para ii, with amenorrhea for one year. Four months after her last menstrual period, there were symptoms suspicious of ectopic pregnancy. In the seventh month, fetal movements were felt by the patient. Laparotomy disclosed a mass attached to the left tube and adherent to the left side of the uterus, which in itself appeared to be normal. Full-term uniovular twins present, one 40 cm., weighing 1,730 gm.; the other 34 cm. long and weighing 1,400 gm.

P. E. Hermanson, 1936. Primipara, married three years. Last menstrual period, approximately five months before death. Fourteen weeks after last menstrual period, there was onset of abdominal pain and vomiting. Admitted nine days later and died with signs of internal hemorrhage before laparotomy could be performed. Autopsy showed two fetuses in the abdominal cavity about three months old. There was a large erosion of the tube.

W. Sawitzky, 1936. Twenty-seven-year-old woman with amenorrhea for fifteen weeks. Two months after her last menstrual period, began to have vaginal bleeding and pain. She was operated upon seven weeks later; laparotomy showed right twin uniovular tubal pregnancy. Embryos were 12 cm. long.

J. Giraud, 1935. Ruptured twin ectopic pregnancy about three months' size. It is not definitely stated whether this was unilateral twin tubal ectopic or bilateral ectopic pregnancy. This and the following case are considered doubtful.

O. Viana, 1935. Thirty-five-year-old multipara. Last menstrual period ten weeks previous to operation. Four weeks after last menstrual period, patient noticed vaginal bleeding and finally sudden abdominal pain and fainting. At laparotomy the left tube was removed; no free blood was found in the peritoneal cavity. Pathologic examination of the specimen showed two cavities, one or which contained an embryo 22 mm. long. The cavity was empty. No actual communication existed between the two cavities. Histologic examination of the septum between the two cavities showed the following sequence of tissue: Amnion, chorion, tubal wall, chorion, amnion. On this a probable diagnosis of twin ectopic pregnancy was made.

CASE 1.—L. B. A., a 28-year-old, gravida v, para i, colored woman was admitted to the hospital on May 29, 1928 with the following history: Her last menstrual period had been six months previous to admission. She had noticed irregular, scanty bleeding for the past five months. On the day before admission, the bleeding became more severe and for the first time had been accompanied by cramplike lower abdominal pain. Prior to her present illness, her menstrual periods had always been regular.

On abdominal examination, a somewhat irregular and very tender mass was felt extending to the umbilicus. Vaginal examination revealed an enlarged uterus, pushed anteriorly and to the left by a large globular, soft, fixed mass, continuous with that felt abdominally.

It was believed that the patient had an intrauterine pregnancy complicated by either a fibroid or an ovarian cyst. Blood count showed a moderate anemia to be present. X-ray of the abdomen was reported as not showing any evidence of fetal parts. She was watched for nineteen days, when in view of the continued pain and vaginal bleeding, a laparotomy was performed. A large cystic mass which was adherent to the neighboring intestines was well walled off containing twin males about four and one-half months in size. Convalescence was uneventful and the patient was discharged sixteen days after operation.

Unfortunately, the pathologic report is incomplete. However, an x-ray taken of the excised specimen shows "the spine, ribs, and long bones of the twin fetuses, very well outlined."

AN INCUBATOR FOR INFANTS

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THE apparatus described contains certain important features not included in other incubators. The fact that it remains closed at all times permits the fulfillment of the following requisites hitherto considered not practicable. (1) An accurate maintenance and adjustment of temperature and humidity permits the selection necessary in such air-conditioning for infants of different weights. (2) The infant may remain without covering or clothes which condition allows great freedom of muscular activity especially for the important function of respiration. This lack of clothes also facilitates handling and prevents the usual alterations in temperature dependent upon covering and uncovering or upon changing the diaper. (3) In addition special gas mixtures, either for emergency or prolonged use, may be provided. (4) Also, a practically complete isolation is maintained against pathogenic microorganisms, whether air-borne or otherwise. (5) It permits the nurse to work in an atmosphere which is comfortable for her. In the ordinary air-conditioned room the optimum humidity and temperature for the infant are too great for the nurse's tolerance.

This incubator is made in two compartments, one above the other. The upper contains the baby, the lower houses the working unit. The upper compartment is an air-tight, heat-insulated chamber. The air for the infant is drawn from out of doors. This air is filtered and humidified before it enters the incubator and it is heated inside the chamber.

The thermostat is calibrated and is adjustable up to 99° F. There is a temperature fluctuation of less than one degree from the selected point.

The humidistat is similarly made and is adjustable up to 100 per cent relative humidity. The humidity will remain within a 5 per cent variation.

The rate of air flow is uniform at all times since it is driven by a one-speed motor. The outside air is drawn in at the rate of 0.4 cu. ft. per min. It passes over the baby at a rate of 30 ft. per min. Under ordinary conditions the air is recirculated about six times, the incoming air being approximately one-sixth of the total air stream. The ratio of recirculated air to outside air is adjustable for use of special gas mixtures. This is accomplished by a valve on the fresh-air pipe. Gas mixtures are admitted through a pet cock on the negative pressure side of the blower. Air samples for analysis are obtained through a pet cock on the positive pressure side of the blower. The waste air is discharged at the same rate the fresh air is admitted whether this be outside air or gas from a tank. These constant conditions are maintained by keeping the chamber closed at all times.

View is obtained into the electrically illuminated interior through the full length window. This is made of two thicknesses of noninflammable celluloid.

The baby is handled through balloon cloth sleeves, elastic about the wrist. These are kept rolled when not in use. Bottles, syringes, diapers, etc., are admitted through an air-lock. This is a boxlike compartment having two doors, one opening into the chamber and one to the outside. Both doors are air-tight. When a bottle is to be given the outside one is opened and the bottle is placed inside the box. The nurse's hands, which are her only contact with the baby, are scrubbed and then introduced through the sleeves to the chamber. The inside door of the box can then be opened and the bottle taken out. One door is always locked so that there is always an air-tight partition between the chamber and the outside air.

Pathological Report.—"Specimen consists of a spherical mass measuring 10 cm. in diameter. The surface shows numerous adhesions and marked hemorrhagic infiltration of the capsule. Upon opening the specimen, there are two fetuses present, having a crown rump length of seven and six centimeters respectively. There is one amnion and one chorion present. Polydactylism can be recognized. No evidence of tubal structure can be identified (Fig. 1). Microscopic examination reveals hemorrhagic placental tissue. Occasional chorionic villi lined by a single layer of Langhans cells are found."

DISCUSSION

Two cases of unilateral twin ectopic pregnancy have been presented. If increase in size of the fertilized ovum had any relationship to the occurrence of ectopic pregnancy, it would seem that the incidence of twins in tubal pregnancy should be higher than that reported. However, the size of the ovum does not seem to be the etiologic factor. Embryologically, it has been shown that the frequency of monochorial to dichorial twins is fifteen times greater in tubal twinning than might be expected from the uterine ratio. It is believed that the high incidence of monochorial tubal twins is due to an abnormal stimulus (inadequate oxygenation or nutrition) given to the fertilized ovum in the tube at the time corresponding to gastrulation.

We believe the etiologic factor causing tubal pregnancy, whether single or twin, to be the same: that is, any change which delays the ovum in its progress through the tube will favor tubal pregnancy. The clinical picture of twin ectopic pregnancy usually resembles that of the ordinary ectopic pregnancy. Not infrequently, however, because of the greater tendency for hemorrhage to occur and cause a larger mass than that ordinarily encountered, a correct diagnosis may be difficult.

These cases have been presented as clinical and embryological curiosities, interesting for their comparative rarity. Including the two cases presented tonight, the total number of reported authentic cases is believed to be 65.

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By employing the thermo-electrical system, the author studied changes of uterine, vaginal, and rectal temperatures following the abdominosacral application of diathermy and the short wave. It was observed that the temperature of the deep organs in the female genital sphere was greatly increased following the application of the short wave. This result was not obtained with diathermy.

AUGUST F. DARO.

margin of safety in the air supply. The second is a control thermostat which would shut off the heater and the humidifier if the temperature should reach 99° F. If this temperature is reached a bell rings which stops ringing only when the temperature has fallen below this level. If the current should fail, the lights, which are on continuously, would go off.

A simple cooling unit and a dehumidifier can be installed if desired, since the incubator is an air-tight, heat-insulated chamber.

Clinical experience with this incubator covers 25 premature babies. Because of the conditions under which the incubator was used this number has been sufficient to evince several striking results. Ten babies were in an incubator while it was kept in a 16-bed ward of older babies where cross-infections were constantly occurring. No attempt at isolation was made. Gowns and masks were not used by the incubator attendants. The only precautionary-measure taken was that of washing the hands with soap and water and rinsing them in a bichloride of mercury

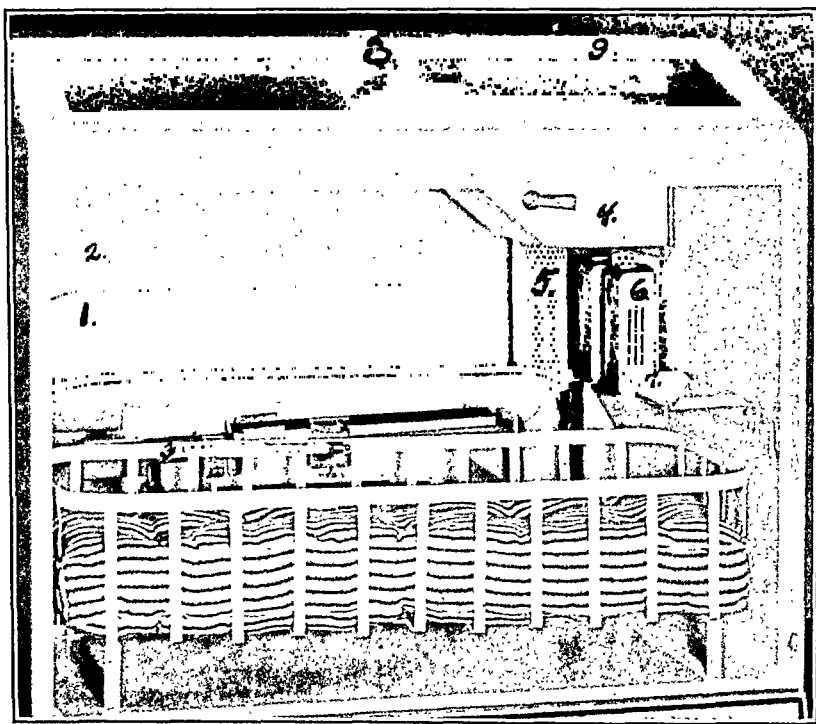


Fig. 2.—Upper compartment, interior: 1, scale; 2, removable gavage bracket; 3, thermometer on the basket-bed; 4, inside air-lock door; 5, heater; 6, adjustable humidistat and thermostat, with the control thermostat between them; 7, removable tray; 8, stopper; 9, outside air-lock door.

solution before starting them through the sleeves to the baby. In this room environment no premature baby in the incubator has had a respiratory infection. Only one of the infants developed diarrhea. This was mild and transient. One baby developed a staphylococcus abscess at the site of repeated hypodermoclysis injections.

It is our feeling that this result was obtained largely by limitation of air-borne organisms as only out-of-doors air is admitted to the incubator. No ward air enters the chamber. However, it must be noted that contact and droplet infection are eliminated as well.

Another result of importance is the absence of cyanotic attacks. In some of the babies between 1 pound and 15 ounces, and 3 pounds, cyanotic attacks occurred suddenly and frequently until the oxygen content of the incubator was raised and its humidity was increased. Oxygen, introduced through the pet-cock for that purpose at 4 liters per minute maintains continuously the concentration of oxygen at 46 per cent. This practice is used for the very small infants. The percentage of oxygen is decreased gradually as the infant grows larger and stronger until it is

A scale is built into the chamber and in addition to its ordinary weighing function is used as an alternate bed while the basket-bed, in which the infant usually lies, is being changed.

An opening in the top of the chamber is closed by a rubber stopper penetrated by a glass tube. Emergency carbon dioxide and oxygen can be delivered here to a tube connected to a mask or funnel inside. A stethoscope can be used with this connection and a burette can be attached with a connecting tube to a needle or rectal tip for the administration of large amounts of fluid.

The incubator is silent since the motor is mounted on rubber and there are only rubber connections between the chamber and the moving parts (motor and blower).

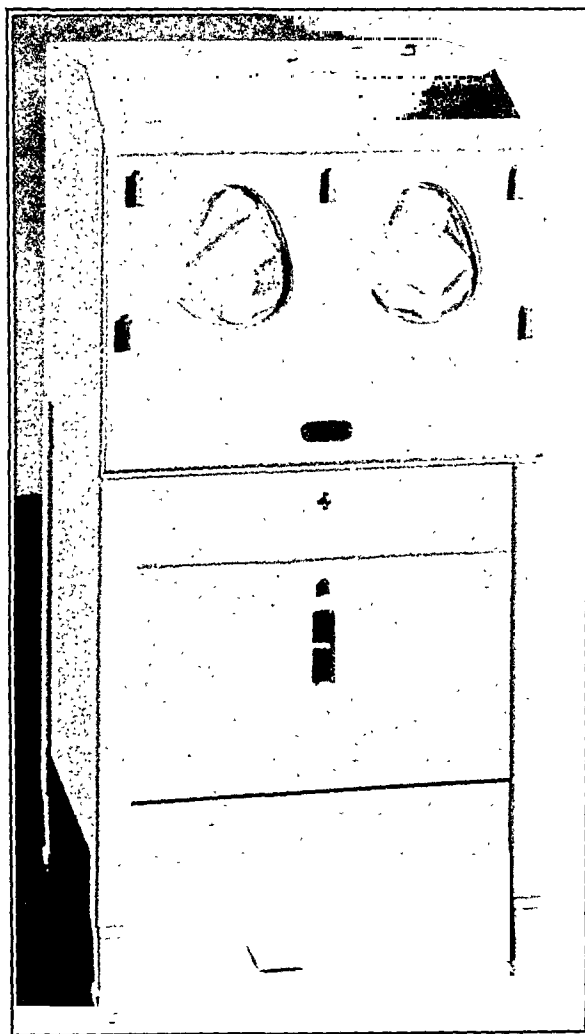


Fig. 1.—Exterior of the incubator; showing the rolled sleeves, water gauge, lighted interior, outside air-lock door, and stopper in the top.

From the nurse's standpoint it is easier to manipulate than other incubators. The mechanism is automatic. The baby is naked, or nearly so, since the conditions of his environment are constant and handling is proportionately simplified. The only care the incubator requires is the replenishment of water to the humidifier reservoir and a monthly oiling of the motor. The reservoir is an ordinary mason jar inverted in a standard. It stands behind a slot in the door of the lower compartment so that it acts as a gauge.

Although the most reliable instruments possible are used, there is always some danger of failure of function in anything mechanical. To guard against any such failures safety devices are provided. The first is an indicator of air-flow. Should the motor fail this would no longer register. There is approximately a four-hour

Nuck. These round ligament tumors frequently include fibromyomas, adenomyomas and endometriomas, fibromas, fibro- (myxo- and myo-) sarcomas (often arising from degenerated fibromyomas), dermoid cysts, and less frequently lipomas, lymphangiomas, varicosities, tuberculous masses and Wolffian body tumors.^{1, 5} Tubal gestation has been reported. When tumors of the other pelvic viscera are added, the variety¹ of neoplasms which may be found in the canal of Nuck is very diverse.

Tumors of the canal of Nuck occur most frequently in the third and fourth decades but may be seen before twenty and after forty. The mass, usually symptomless, is of one to three years' duration and slow growing. Pressure effects of the growth may give symptoms. Endometriomas will often exhibit swelling and pain coincident with menses,² as may an incarcerated ovary.

The mass varies in size from 2.5 to 50 cm. in diameter and has weighed as much as 488 ounces.⁵ Fibromyomata are oval to multilobed in shape and encapsulated. They vary in consistency but may be cystic as are the lymphangiomas and dermoid cysts. Endometriomas are usually hard nodules fixed to adjacent tissue, but may be hemorrhagic and cystic.² The histology varies with the vagaries of the tissue of origin.



Fig. 1.—Papillary cystadenocarcinoma of the canal of Nuck.

CASE REPORT

C. L., white female, 34 years of age, first noted a cystic mass in the left labial region three years ago. The mass trebled in size and was slow growing. Catamenia was normal and the mass was not painful or swollen during menses. Examination disclosed a round cystic tumor in the superior portion of the left labium, 4 by 3 by 2 cm. It was not attached to the skin, or tender. Pelvic examination was negative.

At operation, dissection of a well-demarcated mass in the left labium revealed the upper pole to be associated with a fibrous cord which attached the tumor to the round ligament. Another mass, in the upper part of the canal of Nuck, was identified as a normal ovary. Recovery was uneventful.

Gross Pathology.—The specimen was an ovoid mass, 4 by 3 by 2 cm. The tumor was cystic and contained 15 c.c. of light brown gelatinous fluid. The cyst wall was 5 to 8 mm. thick, and on the inner surface showed fine papillary projections.

Histology (Dr. Harold Gordon).—"Some of the sections are covered by a stratified cornified squamous epithelium with which are associated large sebaceous glands and an occasional thin hair follicle. In the deep corium is a dense fibroelastic band of tissue which is lined by a single row of tall columnar epithelial cells. The

discontinued completely when the baby is approximately $3\frac{1}{2}$ pounds. After this the oxygen tank is left attached to the incubator. At any time should the emergency arise the chamber can be flooded with oxygen instantly by turning the tank valve. In some cases a tube is left attaching an oxygen tank to the glass tube at the top of the chamber. The other end of this glass tube is connected by rubber tubing to a funnel to be put over the infant's face should cyanosis recur.

The percentage relative humidity required by infants under $4\frac{1}{2}$ pounds is high as shown by Blackfan and Yaglou.* In this incubator infants of such weight range were kept in 70 per cent relative humidity. When the percentage was dropped below 65 per cent, cyanotic attacks became frequent in weak infants. This would seem to be due to increased heat loss in the lower humidity range with the resultant increase in their energy expenditures. In none of the infants in the present group have cyanotic attacks occurred when humidity was kept in this high range and when the oxygen was maintained in this high concentration.

Since the temperature and the humidity are so closely controlled the infants are left uncovered and often completely naked. The temperature fluctuation as recorded by rectal thermometer is within a one degree diurnal variation. The activity of the infants under such conditions of freedom from clothes is vigorous. Even at 2 pounds they kick their feet over their heads while lying on their backs and otherwise move freely in less excursive motions. The respiratory function is unhampered by the weight of blankets.

SUMMARY

1. Infection was reduced in premature babies although the incubator was run under most adverse surrounding conditions.

2. Cyanotic attacks were stopped and did not recur when the oxygen content and the humidity of the incubator were kept at a high level.

3. The usual diurnal temperature fluctuation of infants as recorded rectally was less than one degree.

4. Motion including that of respiration was unhampered and was freely indulged in by infants, even to the smallest.

5. The success with this incubator has warranted the building of "cabinet cubicles" or converted incubators for older infants, which embody the same principles of air-conditioning and also isolation from infectious microorganisms.

315 REX AVENUE

PAPILLARY CYSTADENOCARCINOMA IN THE CANAL OF NUCK

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IF, IN embryonic development, the normal separation of the ovarian and the round ligaments by the cornu of the uterus does not occur and fusion ensues, adult pelvic viscera may be found in the canal of Nuck, a persistent peritoneal sac and developmental anomaly, appearing in the anterior abdominal wall at the point of fusion of a band of tissue from the genital fold (anlage of the uterus) and a mesodermal ingrowth from the lateral abdominal wall. Such a ligamentous fusion might result in a developmental descent of the ovary, tube, and ligamentous structures including remnants of the Wolffian body, into the canal of Nuck.

About 400 cases of herniation of pelvic viscera into the canal of Nuck have been reported, the great majority being ovarian and tubal.^{3, 4} Rarely have neoplasms been described but a survey of the tumors involving the round ligament show that many of these masses are extraperitoneal and may find their way into the canal of

*Am. J. Dis. Child. 46: 1175, 1933.

of age. There was no shock, accident, or apparent cause for the cessation of her menses. She remained amenorrheic approximately ten years, until Aug. 23, 1935. During this period, the patient put on considerable weight, going from 97 pounds at the time of her marriage in 1925 to 165 pounds on Jan. 1, 1935. Except for weakness, lassitude, and the gain of weight, there were no other associated, general or menopausal symptoms.

The patient was first seen in December, 1934, complaining of obesity, weakness, amenorrhea of about ten years and sterility. Aside from her menstrual history, there was little to be ascertained. She was never operated upon and had no serious illnesses. Her family and past histories were essentially negative. Her husband was in good health. His semen was tested and found normal.

Physical examination revealed a somewhat obese, middle-aged female in apparently no great distress. The fat was distributed mainly over the abdomen, buttocks, thighs and breasts, and was not extremely marked. Her secondary sexual characteristics were within normal limits with no peculiar distribution of hair. The heart, lungs and abdomen were negative. Vaginal examination revealed a small uterus and a conical cervix. Adnexa were not palpable.

Laboratory findings were essentially negative. The sella turcica was slightly enlarged but within normal limits. Basal metabolism -19.

Hormone tests on blood and urine for five consecutive weeks revealed no estrone. The urine showed absence of follicle stimulating hormone. With these hormonal findings, it was decided that this was a case of secondary amenorrhea probably of pituitary origin.

In January, 1935, patient was given 1 c.c. of antophysin intramuscularly into buttock daily for five days, each cubic centimeter containing 100 rat units.

In February, thirty days after first January injection, patient received 1 c.c. of antophysin intramuscularly into buttock daily for five days. Each cubic centimeter contained 500 rat units. This latter procedure was repeated at thirty-day intervals for five successive months. By this time, the patient had received 15,500 rat units of antophysin over a period of seven months.

On Aug. 23, 1935, patient had menstrual molimina and slight spotting for three days; 2,500 rat units of antophysin were again given over a period of five days, 500 rat units each day and on Sept. 23, 1935, patient again had menstrual molimina, plus slight increase in amount of staining. 2,500 rat units of antophysin were again given in the same manner, and on Oct. 23, 1935, patient had menstrual molimina plus still more bleeding. Continuing the same treatment, a so-called period occurred on November 23. On December 23, no molimina, but spotting for one hour occurred. Up to this time patient had received a total of 25,500 rat units of antophysin. Owing to absence of menstrual molimina and only slight spotting in December, patient was advised to return in two weeks for estrone injections, to be given in conjunction with antophysin. However, at the end of one week, patient complained of severe nausea. Vaginal examination was indefinite owing to obesity and the Aschheim-Zondek test was positive. Patient received no further treatment. Outside of some weakness, inability to get around after the eighth month and slight dizziness, her ante-partum course was uneventful.

On Aug. 22, 1936, she was delivered by low forceps and lateral episiotomy of a living female child. Puerperium was normal and patient nursed her baby for several months. Then due to depleted milk supply and weakness, baby was weaned. It is almost six months since birth of child and patient has not menstruated yet but has had menstrual molimina during past two months. At present, she weighs 167 pounds.

SUMMARY

A female, aged 31, who had amenorrhea for ten years, received 25,500 rat units of antophysin over a period of eleven months in manner stated above, had four menstrual or pseudomenstrual periods, finally conceived and gave birth to a living child.

epithelium forms small papillary proliferations many of which contain hemosiderin laden phagocytes and monocytes. The fibroelastic capsule likewise shows localized areas of lymphocytes and phagocytes. The deeper portions of the tissue are occupied by atypical gland acini growing upon firm irregularly formed stalks of fibrous tissue containing large spindle-shaped myofibrils (smooth muscle). The epithelium on the stalks is tall simple columnar cells with a cuticular margin and showing well defined cilia; some cells are devoid of cilia. In some portions, the epithelium penetrates the fibromuscular stalks but there is no evidence of infiltration of the capsule proper. The appearance is that of a papillary cystadenocarcinoma, in situ, of very low grade malignancy'' (H and E stain).

Weitzman⁶ has described a tumor of the corpus uteri, whose cytology closely resembles this tumor, and he is of the opinion that this arose from the Wolffian body. Such an origin cannot be excluded here. However, it is possible that the neoplasm arose from ovary or oviduct. If tubal in origin, it is supposed that an oviduct might have been identified in the canal as was a normal ovary. Moreover, the wall of the cyst did not contain any bundles of adult smooth muscle characteristic of tubal wall. Again, in papillary neoplasms of the tube, the stroma of the papillae is not found to contain myofibrils. However, Weitzman describes myofibrils in the papillary stalks of his Wolffian body tumor. That this tumor could have arisen from and does resemble closely papillary cystadenomatous neoplasms of the ovary is conceded. Such tumors are common, while tumors of the Wolffian body are very rare despite the fact that simple Wolffian body cysts are not infrequent in routine examination of oviducts. In favor of a Wolffian tumor is the fact that the operator identified a normal ovary in the canal. Roentgenographic studies of the uterus and tubes would do much to rule out a tubal origin, but in the absence of intraperitoneal examination, it is not possible to rule out either an ovarian or Wolffian body origin.

SUMMARY

A case of papillary cystadenocarcinoma of the canal of Nuck in a white female, 34 years of age, is reported. The possible origin is considered.

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CYCLIC TREATMENT OF A CASE OF SECONDARY AMENORRHEA OF TEN YEARS' DURATION

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REPORTS of cases of secondary amenorrhea treated successfully with hormones have appeared in the literature in the past few years. The following case is reported because of (1) The large dose of the follicle stimulating hormone employed. (2) The long period over which the treatment was continued. (3) The cycle adopted for administration of hormonal product used. (4) The successful production of cyclic bleeding followed by conception and later by the birth of a living child.

Mrs. R. L., aged 31 years, married eleven years, had been sterile. Her menses began at the age of 12, and occurred regularly every twenty-eight days, lasting five days. They were associated with cramplike pains on the first two days, and three months after she was married her periods ceased. At this time she was 20 years

differences when tested with homologous and heterologous sera which were valuable in confirming the morphologic and biologic findings. The new species *M. stellatoidea*, for example, differed from *M. albicans* in colony formation on blood agar, in morphologic characteristics on corn meal agar and slight differences in carbohydrate fermentation. Justification for the separation of these species was enhanced by the fact that they were quite different antigenically. Agglutination tests are not necessary for identification and the close serologic relationship of certain species of the genus *Monilia* eliminated this test as a single rapid means of identification.

TABLE I

	DEXTROSE	SACCHAROSE	LACTOSE	MALTOSE	LEVULOSE	DENTRIN	GALACTOSE	MANNITE	INULIN	MILK
<i>M. albicans</i> (Benham)	AG	A	—	AG	AG	AG	A	—	—	clot
<i>Monilia</i> type II (Stovall)	AG	A	—	AG	AG	AG	A	—	—	clot
Vaginal strains (19)	AG	A	—	AG	AG	AG	A	—	—	clot
<i>M. parapsilosis</i> (Benham)	AG	—	—	—	AG	—	—	—	—	—
<i>Monilia</i> type I (Stovall)	AG	—	—	—	AG	—	—	—	—	—
Vaginal strains (3)	AG	—	—	—	AG	—	—	—	—	—
<i>M. candida</i> (Benham)	AG	AG	—	AG	AG	AG	AG	—	—	—
<i>Monilia</i> type III (Stovall)	AG	AG	—	AG	AG	AG	AG	—	—	—
Vaginal strains (4)	AG	AG	—	AG	AG	AG	AG	—	—	—
<i>M. Krusei</i> (Benham)	AG	—	—	—	AG	—	—	—	—	—
Vaginal strains (4)	AG	—	—	—	AG	—	—	—	—	—
<i>M. stellatoidea</i> n. sp. (29 strains)	AG	—	—	AG	AG	AG	—	—	—	clot
<i>Cryptococcus</i> sp. Vaginal strains (9)	AG	—	—	—	AG	—	—	—	—	—

Pathogenicity.—Previous workers^{2, 8} have demonstrated that cultures of *M. albicans* injected intravenously into rabbits cause multiple abscesses and death; five of our strains of this species have been tested with like results. Equal doses of 3 strains of *M. stellatoidea* proved to be incapable of causing abscesses or death in rabbits after intravenous injection.

SUMMARY OF DIFFERENTIAL CHARACTERISTICS

The descriptions given above have been made purposely brief because the criteria of identification have been based on constant differential characteristics obtained by a variety of different methods. A system of identification based on less characteristic variations might be misinterpreted by one not trained in the study of fungi. For example, the chief function of the corn meal agar slide culture is to determine whether or not mycelia are formed and thus differentiate between *monilia* and *saccharomyces* or *cryptococcus*. The structures in the mycelium may be diagnostic when properly interpreted but errors may be made if one relies on this alone. The most important criteria for identification, including only the fermentation reactions of dextrose, saccharose, lactose, and maltose are as follows:

M. albicans: Fairly large dull grayish white colonies on blood agar. Forms acid and gas in dextrose and maltose and acid only in saccharose. Chlamydospores are regularly formed on corn meal agar.

The points of interest in this case are:

1. Menstruation or pseudomenstruation was restored after a ten-year period of secondary amenorrhea.
2. Patient conceived and carried to full term, giving birth to living child.
3. Despite the absence of a cyclic curve of estrone, treatment was attempted.
4. Patient was treated over a period of eleven months. Had treatment ceased at six months or less, the hormonal product would probably have been blamed for failure.
5. Treatment was given at thirty-day intervals, establishing a so-called cycle for treatment.
6. This case is not reported in order to represent the sole type of treatment for all cases of secondary amenorrhea. However, it suggests that we might some day arrive at the proper dosage and proper time of cycle for hormonal treatment of amenorrhea.

302 WEST 90TH STREET

PREGNANCY COMPLICATED BY BILATERAL DERMOID OVARIAN CYSTS

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SEARCH of the literature reveals but 3 reported cases of pregnancy complicated by bilateral dermoid ovarian cysts; all of these patients carried to term with the delivery of normal children. I desire to report one additional case.

Mrs. M. K., aged 33 years, consulted me Nov. 14, 1936, with complaints of continuous aching in both lower abdominal quadrants and amenorrhea since Aug. 23, 1936. Family history was irrelevant. Menses began at 12 years, occurred usually at twenty-eight-day intervals, and lasted four days. She stated that she had had no illnesses of consequence with the exception, that fifteen years previously her family physician had advised her of the presence of bilateral ovarian cystosis but had recommended against operative intervention. Six years ago she had a normal pregnancy and labor completed by prophylactic forceps. Since, she had been troubled intermittently with aching in both lower abdominal quadrants and had had occasional periods of amenorrhea ranging from two to three months. Diagnosis on Nov. 14, 1936, was bilateral ovarian cysts with probable pregnancy. Symptoms increased until Dec. 7, 1936, at which time the pregnancy was three and one-half months, when bilateral ovarian dermoid cysts were removed under ethylene-oxygen-ether anesthesia. The cysts were equal in size, 10 cm. in diameter, and were easily removed. Postoperative course was uneventful and the pregnancy was not disturbed. No endocrine therapy was given and subsequent pregnancy was normal until the beginning of the ninth month. At this time transient generalized edema was noted together with gradual and persistent elevation of blood pressure to the upper limits of normal. Therefore labor was induced (two weeks before full term) by Watson's method and a perfectly normal labor and puerperium resulted. Mother and baby were discharged at six weeks post partum in excellent condition.

Schockaert,¹ in discussing ovarian cysts bearing a corpus luteum verum extirpated during various stages of pregnancy, remarks in summing up that we should "diminish the importance that has been attributed to the corpus luteum verum in sustaining pregnancy." To prove his contention he reports 4 cases of *single* ovarian cyst (bearing corpus luteum verum) complicating pregnancy which were extirpated, and one case which had *bilateral* dermoid ovarian cysts removed in the fifth month of pregnancy. All 5 cases ended normally at term.

E. Levy Solal² reports one case of bilateral dermoid ovarian cysts complicating term pregnancy which was successfully treated by cesarean section and bilateral ovariectomy.

J. L. Faure³ reports one case of a six weeks' pregnancy complicated by bilateral dermoids, with bilateral ovariectomy and preservation of pregnancy until term, when it ended normally.

On the other hand Cottalorda⁴ reports one case of torsion of bilateral ovarian cysts in the second month of pregnancy in which bilateral ovariectomy and hysterectomy were performed, and in contrast to Schockaert, Cottalorda recommends removal of the pregnant uterus when complicated by bilateral ovarian cysts.

CONCLUSION

A rare complication of pregnancy is reported which adds to the evidence already at hand that, in the human being, the corpus luteum vera is not absolutely necessary for the preservation and sustenance of pregnancy. However, in the absence of urgent operative indications, it is recommended that operative intervention be delayed at least until the placenta has approximately matured.

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1801 EYE STREET, N. W.

THECA CELL TUMOR OF THE OVARY

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BECAUSE of the extreme interest noted within recent years in the ovarian tumors affecting the endocrinologic status, the following case report is herewith submitted:

B. A. (No. 77568) aged 34, housewife, white, Russian, was admitted to the Beth Moses Hospital (ambulance) on March 9, 1937 complaining of a sudden attack of pain in the left leg, thigh, and hip, radiating to both lower abdominal quadrants, of five hours' duration. No rise of temperature, nausea, or vomiting was associated with this pain. She gave a history of an amenorrhea of eleven months' duration and she said that she had been observed in the out-patient department for the past ten months for this complaint. Her last visit there had been the day previously when she was advised to enter the hospital since an indefinite fullness had recently been noted in the left vaginal fornix. She had been married 14 years and had two children living and well, and had had no miscarriages.

Menses began at 15, occurred every twenty-eight days and were of four days' duration. About three years ago, she noted her menstrual periods decreasing in amount and duration, and that the intervals were becoming more prolonged.

Her family history was essentially negative.

Physical examination revealed a well-nourished, rather pale and acutely ill white female. Temperature 98.4° F., pulse 100, respirations 24, blood pressure 160/90. Slight hirsuties of forearms, legs, and upper lip was noted. Upon abdominal examination, distinct tenderness and slight rigidity were noted over both lower quadrants. No masses were felt. Vaginal examination revealed a normal vulva covered with a thick glairy discharge. The uterus was not definitely outlined due to the rigidity. The uterus, however, felt small and in retroversion, with the cervix pointing toward the symphysis pubis. A rather indefinite fullness was noted in the left fornix.

In view of her generally good condition after admission and since she had been seen in the clinic on the previous day, it was deemed advisable to further study the patient before operation. The following tentative diagnosis was made: (a) Twisted ovarian cyst, (b) chronic salpingitis, (c) microcystic ovaries. The next day, with the patient feeling decidedly relieved, examination was more easily performed and a definite mass about the size of an orange was felt upon bimanual examination, occupying the suprapubic area and distinctly separated from a small uterus. No abdominal tenderness and rigidity were noted at this examination.

The urine examination was negative. Blood (admission) hemoglobin 76 per cent, R.B.C. 3,200,000, W.B.C. 20,000, polymorphonuclears 92, and lymphocytes 8. The sedimentation rate was one hour and thirty minutes. Smears were negative for gonorrhea. Blood chemistry: sugar 80, urea nitrogen 20, uric acid 3.9, and cholesterol 250. Friedman test was negative and Wassermann, negative. X-ray (flat plate): Soft tumor tumefaction occupying suprapubic area.

With the patient refusing further cooperation in studying her case, it was decided to laparotomize her on March 15, 1937, with a preoperative diagnosis of a

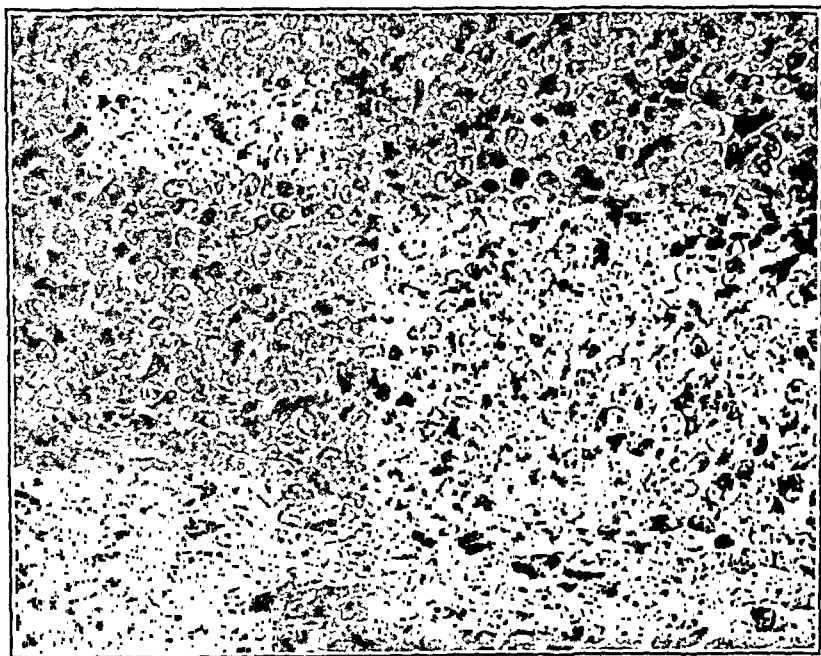


Fig. 1.

left twisted ovarian cyst, probably a persistent corpus luteum cyst. This was done under spinal anesthesia through a median suprapubic incision with the following findings: A small amount of free blood and clots were present. Uterus was regular and normal in size. Right adnexa were grossly normal. Left ruptured ovarian mass about the size of a small male fist of almost solid consistency and of an extremely friable nature. Some of this tissue lay free in the abdominal cavity. There were no peritoneal implantations. Left oophorectomy was performed, and frozen sections taken at this time were reported as those of a benign ovarian tumor. Postoperative endometrial biopsy was unsatisfactory and therefore not reported.

Her postoperative course was entirely uneventful and the patient was discharged on the fourteenth postoperative day.

Pathologic Report (No. 6361).—Gross: Specimen consisted of a mass of tissue distinctly encapsulated and presenting a smooth capsule. The mass was approximately the size of a grapefruit. It contained a jagged rent approximately 10 cm. in length, the margins of which contained considerable quantity of fluid and clotted blood. The surface presented a bosselated appearance. The bosses ranged up to 4 cm. in diameter. A golden yellow tissue with a number of cystic areas was present. In areas, the tissue presented a trabeculated appearance. The central portion was

cystic and contained considerable fluid and clotted blood. This opened through the jagged laceration previously noted. The tumor weighed 331 gm., of which 230 gm. were taken for biochemical assay.

Microscopic.—The mass consisted of very cellular, interlacing fascicles of spindle cells. In the main, the Van Giesen showed no pink fibrils although there were a few small scattered areas in which these fibrils were noted. These areas also showed silver staining fibrils. The nuclei showed slight atypism and mitotic figures were present in a few areas, 2 to 5 per high power field. The cellular appearance was vacuolated and revealed with sudan III considerably finely scattered fat droplets. Under polarized light, a very considerable number of doubly refractile crystals of no specific shape were noted within the cells, as well, apparently, as outside the cells. A number of cystic and hyaline areas were present. A few scattered rosettes were noted in the very cellular areas.

Diagnosis.—Ruptured cellular theca cell tumor of the ovary (left).

Personal communications from the patient reported her as menstruating regularly and with her first period occurring exactly one month postoperatively.

DISCUSSION

Loeffler and Preisel,¹ Melnick and Kanter² and S. H. Geist³ have within recent years called attention to and described a distinctly new type of ovarian tumor characterized by definite histologic, chemical, clinical and endocrinologic characteristics. Though closely related to the granulosa cell tumors of the ovary as described by Robert Meyer, sufficient points of difference have been described to definitely separate them. But 4 of the 22 cases reported to date have occurred in young women with amenorrhea, the usual picture being one of postmenopausal bleeding. They are usually benign, only one of Loeffler and Preisel's cases being described as malignant, and have been shown to secrete theelin in even greater amounts than the placenta. Oophorectomy usually suffices to cause a regression of symptoms.

SUMMARY

A definite case of a ruptured theca cell tumor of the ovary occurring in a young woman and characterized by a prolonged amenorrhea is hereby reported. With oophorectomy, there was a complete regression of symptoms. It is our hope to report, at a later date, the results of a biochemical assay of this tissue.

REFERENCES

- (1) *Loeffler and Preisel*: Beitr. z. path. Anat. u. z. allg. Path. 90: 199, 1932. (2) *Melnick and Kanter*: AM. J. OBST. & GYN. 27: 41, 1934. (3) *Geist, S. H.*: AM. J. OBST. & GYN. 30: 480, and 650, 1935.

789 ST. MARKS AVENUE.

Wharton, Lawrence R.: The Criteria of Cure of Gonococcal Infections in Women, Am. J. Syph. Gonorr. & Ven. Dis. 21: 593, 1937.

The author discusses the criteria by which he has determined that 15 of these 17 patients have been cured.

(1) Long observation through the various stages and final localization of the disease, and the knowledge that these infected foci have been either excised surgically or destroyed completely by the actual cautery. (2) Repeated follow-up examinations with negative findings, for one year. (3) Repeated negative smears. (4) Continually negative history of infection, both personal and marital. There is no single, simple, easy test which will infallibly indicate the presence or absence of gonorrhea.

This series includes women with practically every form of gonorrhea. The author states that after adequate and sufficient treatment and follow-up examination approximately 90 per cent of these patients are well. Some have married and borne healthy children without any infection of either husband or wife. On the basis of this experience, it is evident that gonorrhea in women can be cured.

C. O. MALAND.

UTERINE BAG INTRODUCER

P. GRAFFAGNINO, M.D., NEW ORLEANS, LA.

(From the Louisiana State University, Medical Center.)

THIS simple contrivance has been used in our service for the past two years, and has been found very satisfactory not only for introducing balloon dilators, but also for packing the cervical and uterine canal when indicated.

In this device the end of the Jolly dilator No. 10 (French 27-30) has been cut off, allowing dilator No. 9 (French 24-29) to act as an obturator, while No. 10 acts as a cannula. The Vorhees' bag No. 6 is the largest used, and it is easily introduced through the cannula with uterine dressing forceps after proper folding.

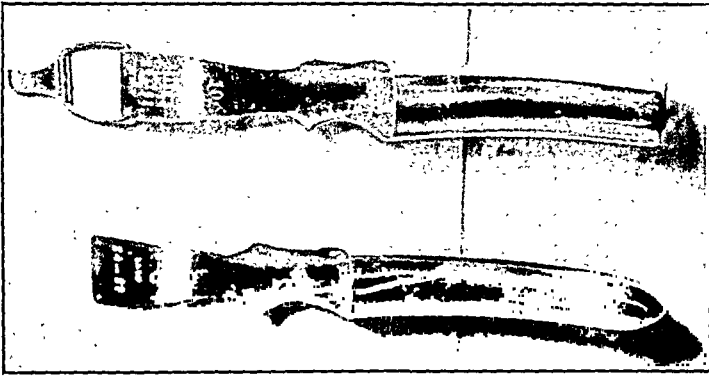


Fig. 1.—Jolly dilator No. 10 used as a cannula and the Jolly dilator No. 9 used as an obturator.

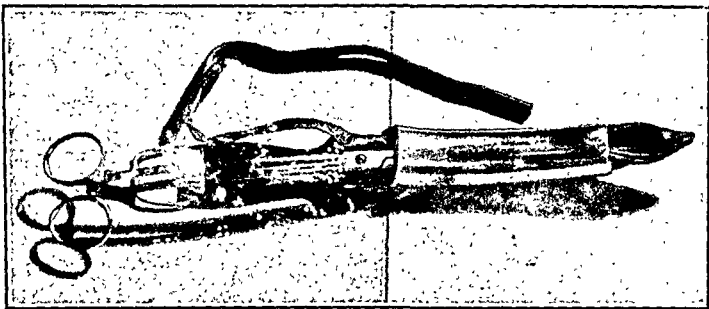


Fig. 2.—Jolly dilator No. 10 with uterine dressing forcep and No. 6 Voorhees' bag.

After preparing the field for operation, the cervix is grasped anteriorly and posteriorly with Smith's hooks. Dilatation of the cervix is begun, using a No. 1 Jolly dilator and continuing in sequence to the No. 10, which is introduced with its obturator. The obturator is now withdrawn and the Voorhees, Barnes', etc., bag is inserted properly folded. Twenty to 50 c.c. of sterile water are instilled in the bag and the introducer is withdrawn. The bag is then filled.

Advantages.—(1) It permits bag introduction with a minimum of trauma. (2) The cervix does not have to be re-dilated as so often occurs when no instrument holds the canal open. (3) It is of great value for tamponing of the uterine canal.

Special Articles

MATERNAL AND FETAL MORTALITY IN A GENERAL HOSPITAL

WHERE THE MAJORITY OF THE OBSTETRIC WORK IS BEING DONE
BY THE GENERAL PRACTITIONER*

PAUL C. FOX, B.S., M.D., F.A.C.S., OAK PARK, ILL.

PRACTICALLY all of the published statistics dealing with maternal and fetal mortality are from strictly lying-in hospitals, or from hospitals where the "maternity staff" is composed entirely of men who have specialized in obstetrics. In these hospitals the general practitioner is not permitted to work, or if so, only by courtesy and under the supervision of the attending staff. It, therefore, seemed that it would be interesting to report the statistics from a general hospital, where most of the confinements are attended by doctors in general practice. There are many such hospitals scattered throughout this country and no doubt if their statistics were taken collectively, they would comprise the vast majority of maternity statistics. Should such statistics become available, we would then have a more accurate picture of hospital maternity statistics than we have today.

It is hoped that the publishing of this report may stimulate other general hospitals to come forward with similar reports, so that the public, or at least the medical profession may be informed as to just how their community hospital stands in regard to maternity work.

Much has been written in recent years concerning the deplorable situation existing in this country in regard to maternal and fetal mortality. No one will deny that there is room for improvement, and we will all agree that every conscientious physician and all first class hospitals must make every possible effort to improve this situation. However, if one is to believe what has been published in the lay press, the General Hospital has been blamed for more than its share of responsibility, and has been placed in a very unfavorable position.

It has been said that "home delivery, even under the poorest conditions is safer than hospital delivery," also that "delivery by a midwife is safer than by a doctor," and again, "the general hospital is a veritable cesspool of puerperal infection." And many other equally damaging remarks have been broadcast to the public in a very dramatic manner. Certainly if such remarks are true and if such conditions do really exist it is high time that we were knowing about it and doing something about it.

This report then, is made with the purpose of showing that not all general hospitals should be so condemned, and that in a well-regulated general hospital it is possible to obtain results which compare favorably with those obtained by the strictly Maternity Hospitals which are justifiably upheld as being ideal.

*Read at a meeting of the Chicago Gynecological Society, May 21, 1937.

In order to understand the significance of this report we must first describe the hospital. The West Suburban Hospital in Oak Park is a general hospital with a capacity of 400 beds. It is situated in a community where 97 per cent of the confinements take place in hospitals and only 3 per cent are home deliveries. However, this hospital draws patients from all of the west side and the west suburban districts of Chicago. There are about 300 physicians who bring patients to this hospital, therefore, it could really be called an open hospital. However, there are certain requirements necessary for regular attendants.

Great importance is given to the Obstetric Department at the West Suburban Hospital. This department is conducted as three distinct units. First, the delivery rooms, which are all well equipped with every modern convenience, are in charge of a supervisor and her assistants who have nothing to do with any other patients except those in labor. Second, the lying-in floor, with its own supervisors, admits no other patients except those who have been confined, or who are in waiting. Any patient developing a temperature from any cause whatever is immediately moved to another floor in the hospital. And third, the nursery, with its own supervisors, is adequately equipped for the care of the newborn. Separate rooms are maintained for isolation of infants when necessary.

The entire department is under the direction of the obstetric committee, which is composed of eight members of the attending staff. Great credit for the good results is due to Dr. Louis Faulkner who has been chairman of this committee during the past twelve years. A standardized technique has been adopted for use in the delivery rooms, and is required of all attendants. The nurses are highly trained in the use of this technique and carry out all the details in every case. So that even though the attendant may not be versed in modern aseptic technique, he finds that his patient receives the advantage of it nevertheless.

Consultation is encouraged in every way possible. It is understood that no serious operative procedure should be undertaken without first having someone in consultation. This is not required, but is strongly advocated. Every effort is made to make these consultations available without embarrassment to the doctor or patient. Members of the obstetric committee hold themselves in readiness to give these consultations regardless of whether or not the patient can afford the consultation.

Table I gives the summary of the data concerning the hospital. This summary shows that 93.5 per cent of the attendants are in general practice, and that 76.8 per cent of the patients were confined by general practitioners. This report could then be looked upon as a report from a general practitioners' hospital. It is interesting to note the relatively large number of physicians. If the cases were equally divided among the attendants it would mean about eight cases for each during the year. However, this is not the situation as there were many of these attendants who had only one or two cases. It is the attending man who takes only an occasional obstetric case who is most likely to run into trouble. These facts are important to keep in mind when judging this report.

TABLE I. SUMMARY OF DATA

West Suburban Hospital Year 1936	400 Bed General Hospital
Physicians Attending Maternity Cases	139
General practitioners	130 or 93.5%
*Special practitioners	9 or 6.5%
Total Number of Confinements	1,193
By general practitioners	915 or 76.8%
By special practitioners	278 or 23.2%

Tables II and III give the details of the work done during the five-year period, 1932 to 1936 inclusive. It so happens that this period includes the year in which the poorest results, and the year in which the best results, were obtained, since the hospital has been in operation. It can therefore be taken as a fair average.

It will be noted that there were 5,568 confinements in the five-year period or an average of 1,114 per year. The average number of attending physicians was 159, again showing a relatively large number of attendants compared to the number of confinements.

The rest of Table II gives general data which are very much the same as occurs in practically any large number of confinements. The premature deliveries shown here include 193 premature infants who left the hospital in good condition, 63 premature neonatal deaths, and 72 premature stillbirths.

The presentations are about as would be expected, being approximately 95 per cent cephalic, 4 per cent breech, and 1 per cent transverse.

Placenta previa occurred in 37 or 0.6 per cent, and ablatio placentae in 16 or 0.2 per cent of the patients. This is somewhat out of proportion as compared to other statistics. It is probable that some cases of ablatio placentae with external bleeding were classified as previa.

In the toxemia group, all patients admitted to the hospital with hypertension or albuminuria or both, were classified as pre-eclampsia; those developing convulsions were classified as eclampsia, and only those whose previous history justified it, were classified as nephritic toxemia.

Table III gives the method of delivery.

All axis traction forceps were classified as high forceps. This may not be absolutely accurate, because some men use axis traction forceps in the midplane. However, it is interesting to note that the incidence of high forceps has markedly decreased in the last several years. In 1936 there were only one-half as many as in 1932, with approximately the same number of cases. Also the incidence of low and midforceps has proportionately increased. This probably means that the attendants are waiting longer before applying forceps. At least it is hoped that this is the explanation.

It is also interesting to note that the incidence of cesarean section is comparatively low. It is commonly believed that the use of cesarean section is abused in general hospitals. Here we see the incidence is 132 sections in 5,568 confinements or only 2.35 per cent. A comparison of these figures will be shown on another chart.

Table IV shows the maternal mortality and causes of death. As previously stated, the year with the poorest and the year with the best

*Practice largely or entirely limited to Obstetrics and Gynecology.

TABLE II. GENERAL DATA

YEAR	NO. PHYSICIANS	CONFIRMATIONS		TWINS	BABIES DELIVERED	TERM	PREMATURITY*	PRESENTATION			PLACENTA		TOXEMIA		
		MULT.	PRIM.					CEPH.	BREECH	TRANS.	PREVIA	ABLATIO	PREEC-LAMP-SIA	EC-LAMP-SIA	NE-PIRIT-IC
1932	165	599	558	13	1170	1110	60	1119	50	1	4	3	26	4	1
1933	172	552	465	7	1024	954	70	978	45	1	6	3	22	4	1
1934	158	493	563	9	1065	990	75	1014	49	2	10	-	23	5	4
1935	161	560	596	19	1175	1108	67	1119	55	1	10	6	30	6	-
1936	139	551	631	11	1193	1137	56	1133	59	1	7	4	9	2	3
Average		2755	2813												
Total	159	5508	5913	59	5627	5299	328	5363	258	6	37	16	110	21	9

*72 Stillborn; 63 neonatal deaths; 193 living.

TABLE III. METHOD OF DELIVERY

YEAR	TOTAL DELIVERIES	SPONTANEOUS	FORCEPS			BREECH EXTRACTION	VERSION AND EXTRACTION	CESAREAN SECTION	CRANIOTOMY	DECAPITATION
			LOW	MID	HIGH *					
1932	1170	952	75	49	16	50	5	23	-	-
1933	1024	795	103	32	11	45	7	29	2	-
1934	1065	820	88	65	6	49	8	29	-	-
1935	1175	904	94	79	6	55	11	30	-	-
1936	1193	906	126	68	8	59	3	21	1	1
Total	5627	4377	486	293	47	258	34	132	3	1

*All axis-traction forceps were classified as high.

results are included. In 1932 there were 7 deaths in 1,157 confinements, or an incidence of 0.60 per cent; while in 1934 there was only one death in 1,056 confinements or 0.09 per cent. The total for the five years was 19 deaths in 5,568 confinements or 0.34 per cent. This compares favorably with results published by other hospitals, which will be shown on another chart.

TABLE IV. MATERNAL MORTALITY AND CAUSES OF DEATH

MATERNAL MORTALITY				CAUSES OF DEATH			
YEAR	TOTAL CONF.	DEATHS	PER CENT				
1932	1157	7	0.60	Toxemia	5	Infection	1
1933	1017	4	0.39	Eclampsia	3	Cardiac disease	5
1934	1056	1	0.09	Nephritic	2	Embolism	2
1935	1156	5	0.43	Hemorrhage	4	Inversion of	
1936	1182	2	0.16	Atony	1	uterus	1
Total	5568	19	0.34	Placenta		Pneumonia	1
				previa	1		
				Ablatio pla-		Total	19
				centae	2		

There were two deaths in the original report which are not included, one death in 1932 due to a ruptured duodenal ulcer, and one in 1933 due to a brain tumor. Both of these cases were proved by autopsy, and are certainly not puerperal deaths.

In considering the causes of death, we find that toxemia and hemorrhage, as usual, head the list of etiological factors, having caused 9 of the 19 deaths in this series.

There was only one death due to septicemia or puerperal infection. This followed a cesarean section in a neglected case. Evidently there is no evidence of a "cesspool of infection" in this general hospital.

The incidence of deaths due to cardiac disease seems relatively high. It is possible that the method of management of these cases is at fault. Perhaps a closer cooperation with the internists is needed, or perhaps more careful prenatal care is indicated. This might also apply to the toxemia group.

Table V shows the infant mortality. The incidence of 255 infant deaths from all causes in 5,627 deliveries gives us 4.5 per cent infant mortality. This also compares favorably with other hospitals. Here again we see that prematurity is the one great predisposing cause of the relatively high infant mortality. Approximately 50 per cent of the

M. parapsilosis: Small round pearly white colonies on blood agar. Forms acid and gas in dextrose.

M. candida: Wide mycelial fringe around colony on blood agar. Bubbly surface growth in Sabouraud's broth. Forms acid and gas in dextrose, saccharose and maltose.

M. Krusei: Wide dry "collarlike" surface growth on Sabouraud's broth. Variation in size and shape of colonies on blood agar. Forms acid and gas in dextrose.

M. stellatoidea: Stellate colony on blood agar. Ball-like clusters on corn meal agar. Forms acid and gas in dextrose and maltose.

Cryptococcus sp.: Meager growth on blood agar. Fails to produce mycelia on corn meal agar. Produces acid and gas in dextrose.

DISCUSSION

The significance of the presence of yeastlike organisms in certain types of vulvovaginitis has been discussed elsewhere.⁹ The lack of agreement on methods of identification and suitable terminology has caused confusion and has made it difficult to compare results of the different clinics working on similar problems. A satisfactory agreement is possible only when the technical methods are adapted to the resources of the ordinary hospital laboratory, and when the criteria upon which identification is based are sufficiently distinctive to be obvious to the technician without mycologic training. This has been kept in mind in working out the above procedures for identification. The same methods have been applied with equal success to approximately 100 additional strains of *monilia* isolated from other parts of the human body.

The new species *Monilia stellatoidea*, which is so similar to *M. albicans* when grown on Sabouraud's medium, may be of significance in the interpretation of certain clinical findings. This fungus which occurs frequently in the vagina (43 per cent in our series) has been shown to be nonpathogenic for rabbits and may be a harmless parasite in the human vagina. Many of the yeasts formerly identified as *M. albicans* may prove to be *M. stellatoidea* and thus explain why vulvovaginitis occurs in only about half the patients from which the so-called *Monilia albicans* has been isolated.⁹

According to the rules of botanic nomenclature, a previously undescribed fungus cannot be officially recognized unless a concise Latin description is appended.

Monilia stellatoidea n. sp.: Found in vaginal secretions of pregnant or nonpregnant women. Colonies stellate on beef-extract blood agar incubated at 37° C. for ten days; thick creamy colonies on Sabouraud's dextrose agar at room temperature. Broth clear with heavy sediment. Forms acid and gas in dextrose, maltose, levulose or dextrin; milk coagulated. Large clusters of ovoid and round conidia formed at septations along pseudomycelium on corn meal agar at room temperature; chlamydo-spores very rare. Nonpathogenic for rabbits.

Habitat in secrementis vaginalibus feminarum praegnantium aut non-praegnantium. Coloniis vescentibus agare carnis atque cruoris, decem dies, aestate 37° C., et formatis

with those of a well-equipped general hospital. This is done because we all expect the maternity hospitals to set the standard.

It will be noted that in making this comparative table, one year has been used for each of the maternity hospitals, and two years for the West Suburban Hospital. This was done so that the total number of cases handled would be somewhere near the same.

The striking fact brought out in this comparison is that both the maternal and fetal mortality in each institution is very near the same, the West Suburban Hospital being slightly less than that of the Boston Lying-in, and slightly greater than that of the New York and the Chicago Lying-in Hospitals.

It is interesting to note that the percentage of cesarean sections performed is less in the general hospital than it is in the maternity hospitals. This comparison is made because it seems to be the common opinion that general hospitals abuse the use of cesarean section. This has proved not to be the case with this particular hospital.

Unfortunately it is impossible in a paper of this kind to review the statistics of all general hospitals, and unfortunately all general hospitals may not be able to come up to this standard. So that the criticism may be made that the West Suburban Hospital is the exception rather than the rule. However, there can be no doubt that there are hundreds of general hospitals in this country which could show equally good results.

The fact remains that the majority of confinements always have been, and probably always will be, conducted by general practitioners. In recent years most of these confinements have been conducted in hospitals, and of necessity these hospitals have been general hospitals. It is impossible to establish well conducted lying-in hospitals and maternity centers in every community. It is also impossible for every maternity case to have the advantage of a highly trained specialist.

It would seem therefore, that our problem is to teach and train our medical students and interns, most of whom will be general practitioners, in such a manner that they will be competent to conduct maternity cases. This point cannot be too strongly emphasized especially in these days when many of our medical schools seem to be reducing the number of hours devoted to instruction in obstetrics. The second important problem is to conduct and regulate the general hospitals in such a manner that the general practitioner will have proper facilities with which to do his work. All hospitals accepting maternity cases should be compelled to meet certain requirements and should be required to report their maternal and fetal statistics. This would stimulate a greater interest in this department of the hospital and help to give obstetrics the important place it deserves. Too often, at the present time, it seems that the obstetric department of the general hospital is given the least consideration. When surgery, medicine, x-ray, et cetera, have been given all the space and equipment they need, then the obstetric department may have what is left. Where such conditions exist it will be impossible for the general hospital to obtain satisfactory results.

This report, we believe, clearly demonstrates that in a properly equipped and properly managed general hospital, where maternity

infant deaths were premature infants. The hospital has furnished every modern facility for the prevention of these deaths, such as resuscitation apparatus, respirators, and incubators. Were it not for this equipment, no doubt the infant mortality would be still higher. However, the prevention of premature delivery is the important problem.

TABLE V. INFANT MORTALITY

YEAR	BABIES DELIV- ERED	STILLBORN		NEONATAL		TOTAL		TOTAL	PER CENT
		FULL TERM	PREMA- TURE	FULL TERM	PREMA- TURE	FULL TERM	PREMA- TURE		
1932	1170	19	16	9	14	28	30	58	4.9
1933	1024	17	15	9	12	26	27	53	5.2
1934	1065	13	13	5	12	18	25	43	4.03
1935	1175	19	14	9	14	28	28	56	4.7
1936	1193	14	14	6	11	20	25	45	3.7
Total	5627	82	72	38	63	120	135	255	4.5

Other details of the causes of infant deaths have been omitted because they represent the general run of causes, such as cerebral hemorrhage, monstrosities, et cetera, and need not be repeated here. These details, however, are available.

A comparison of these statistics with those of the Boston Lying-in Hospital, the New York Lying-in Hospital and the Chicago Lying-in Hospital is shown in Table VI.

TABLE VI. COMPARATIVE MORTALITY STATISTICS

HOSPITAL	YEAR	MATERNAL			FETAL					CESAREAN SECTION	PER CENT
		TOTAL CONF.	DEATHS	PER CENT	BABIES DEL.	STILLBORN	NEONATAL DEATHS	TOTAL	PER CENT		
Boston Lying-in	1935	2728	10	0.36	2762	69	68	137	4.9	116	4.25
New York Lying-in	1936	2653	6	0.22	2688	77	33	110	4.09	96	3.6
Chicago Lying-in	7/1/1935 to 7/1/1936	2394	5	0.21	2425	59	43	102	4.2	138	5.76
West Suburban	2 years 1935 and 1936	2338	7	0.29	2368	61	40	101	4.3	51	2.2

Deaths due to abortion, etc., not included. Previae infant deaths not included.

NOTE: Two years 1935 and 1936 are taken for the West Suburban Hospital, so that the number of confinements handled would be as nearly equal as possible.

In making comparisons of one set of statistics with those of another, one often meets difficulties. It is necessary to take a number of factors into consideration. The type of patients handled may be entirely different; the number of cases reported may vary greatly; et cetera.

This comparison is not made with any intention of criticism of the Maternity Hospitals, but rather to show what can be done by properly conducted general hospitals. Here we have taken three outstanding maternity hospitals in this country and have compared their statistics

at the north end of the same floor. In the delivery department the space is apportioned as follows: supervising nurse's corridor, sterilization room, preparation room, doctors' dressing and waiting quarters, two labor rooms and three large well-lighted delivery rooms.

The nursing force consists of three separate units supervised by the head nurse of the department. In the delivery department she is assisted by one graduate and three senior student nurses; on the maternity floor by two graduates and 6 to 9 students, and in the nursery by two graduates and an adequate number of student nurses.

A day and a night intern are assigned to the service and are restricted to this service for three months. Under normal conditions each intern is present at about 150 deliveries during the term of his service. There is a house rule requiring an attending physician to be present at each delivery. In case of necessity any available attending man may be asked to supervise the delivery if the regularly engaged physician cannot be present. This ruling is strictly adhered to and is at variance with the routine in most teaching hospitals where the intern has charge of the delivery of normal service patients. The hospital considers the ruling a desirable safeguard which in no way mitigates against the value of the intern's training.

The Evangelical Hospital may be designated as "open" so far as its staff is concerned. One intern has reported that during his obstetric service he assisted 85 different physicians with the delivery of about 250 patients. The large majority of the younger attending men have received their intern training at this hospital. Many of them have located within a radius of several miles from the hospital and are sending obstetric work to the department. Those in need of advice, consultation, and assistance feel free to call upon their seniors and former instructors. The staff feels that the majority of the younger men has had a good training and their efforts should bear out the contention that a general hospital so equipped and manned can produce results that tend to reduce the present high general mortality rate very considerably.

During the period from January, 1932, to April 1, 1937, the hospital admitted 5,724 women whose condition was in some way associated with pregnancy. Of these 5,232 had deliveries of viable children, 438 aborted or delivered nonviable fetuses, 51 had ectopic pregnancies. Two patients who died were admitted post partum and the remaining one died undelivered.

In the whole group there was a total of 25 deaths. Of these: 13 had delivered viable babies, 7 had aborted, 2 had ectopic pregnancies, 2 were septic cases admitted after delivery and one was a surgical patient dying undelivered. These constitute a gross maternal death rate of practically 0.44 per cent or a ratio of 44 per 10,000 mothers involved. To one familiar with the much better mortality rate in the actual delivery department of the hospital this ratio was distressingly high, and led to a brief comparison with other compilations.

It is interesting to note that even those of us who oppose the correction of gross mortality figures, consciously or unconsciously, do a little detectable tampering with either the numerator or the denominator in our calculations. In a total of 4,387 obstetric discharges Stander includes 412 patients discharged before delivery and 95 patients admitted post partum or not pregnant, and thus arrives at the remarkably good ratio of about 16 deaths in 10,000 patients. De Lee in his last report

work is given the importance it deserves, it is possible for the general hospital to show results which compare very favorably with those reported by the strictly maternity hospitals.

More work along the lines above suggested will be of far greater value in improving our national maternity statistics than destructive criticism, such as has been broadcast through the lay press, which tends to undermine the faith of the public in the medical profession.

715 WEST LAKE STREET

ANALYSIS OF OBSTETRIC MATERIAL OF THE EVANGELICAL HOSPITAL OF CHICAGO*

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THE object of this analysis is the presentation of maternal and infant mortality figures from the Obstetrical Department of the Evangelical Hospital where the greater part of the work is done by general practitioners. During the past few years a number of statistical reports has been published by hospitals in the smaller cities of the United States, but very little information has come from the so-called "non-teaching community" hospitals in the larger centers of population. The program committee of this society has expressed a desire to have short reports presented from institutions of this type doing a fairly large amount of obstetric work. In the time allotted to these reviews a detailed exposition is out of the question, but an attempt will be made to give the essentials as a possible basis for comparative study by other types of hospitals doing similar work.

The advisability of incorporating an obstetric department in a general hospital has frequently been questioned, especially by those practicing in institutions admitting only maternity patients. Williams and Stander have both emphatically expressed the opinion that a separate building is not necessary provided the space allotted to confinement work is properly isolated. To be sure accidental factors may harmfully influence the results in either type of hospital, but their control is dependent upon perfection of technic rather than upon the use of a separate building.

The Evangelical Hospital is recognized by the American College of Surgeons as complying with the standards for hospitals taking obstetric patients. It has a capacity of 200 adult beds and 60 bassinets. The fourth floor is used exclusively for obstetric patients and newborn babies. The 32 adult beds on this floor are distributed among private, semi-private, and small ward rooms. All wards are limited to four beds each. The nursery consists of three bassinet rooms, one of which is used for isolation purposes. In addition there are the usual work and preparation rooms as well as demonstration facilities for mothers' instructions by nurses. The nursery is equipped with four incubators for weak and premature infants. Mothers who for any reason lose their babies are usually removed to another floor. Morbidity patients are cared for in private rooms or removed to a separate floor.

The delivery department is at the south end of the fifth floor, and constitutes an entirely separate unit from the surgical department which is

*Read at a meeting of the Chicago Gynecological Society, May 21, 1937.

stitutes an orderly well-planned and highly efficient department. In the 5,232 mothers cared for, the pregnancy had advanced to the twenty-eighth week. There were 47 sets of twins in the group, making a total of 5,279 babies born.

The type of delivery in the series is stated in relation to the number of babies born. There were 4,031 normal deliveries (76 per cent); 892

TABLE II. INFANT MORTALITY FACTORS

	BABIES	BABIES' DEATHS	STILLBIRTHS	TOTAL DEATHS	PREMATURES			
					BORN	DIED	STILLBORN	ALIVE
Total	5,279	96	135	231	227	29	36	162
Per cent		1.8	2.5	4.3	4.3	13	16	71
Ratio per 1,000		18	25	43	43			

forceps (17 per cent); 273 manual (5 per cent); 83 cesarean sections (1.5 per cent), an incidence of 157 per 10,000. There were two deaths following cesarean section, one in a case of placenta previa, the other in a case of toxemia with eclampsia.

There were 13 maternal deaths among the 5,232 mothers delivered, a percentage of 0.25 or a ratio of 25 per 10,000. The accepted causes of these deaths and the type of delivery are as follows:

Toxemia, abruptio placentae	(spontaneous)	1
Abruptio placentae, hemorrhage	(forceps)	1
Toxemia, eclampsia	a. cesarean section	1
	b. forceps	1
Placenta previa, peritonitis	(cesarean section)	1
Placenta previa, hemorrhage	(version)	1
Sepsis, pulmonary embolism	(forceps)	1
Thrombocytopenic purpura, hemorrhage	(spontaneous)	1
Chronic endocarditis, decompensation	(forceps)	1
Shock (sudden death not due to hemorrhage)	(forceps)	1
Pulmonary embolism (1 hour after 3rd stage)	(spontaneous)	1
Gangrenous appendicitis at term	(spontaneous)	1
Pneumonia (antepartum)	(spontaneous)	1

Of the 5,279 babies born in the viable period there were 96 neonatal deaths including the 29 deaths among premature infants. If to these are added 135 stillbirths the total infant mortality is 231 or 4.3 per cent, a ratio of 43 per thousand. There were in all 227 premature viable babies of whom 36 were stillborn, 29 died and 162 were discharged alive.

This brief study of the factors influencing maternal and fetal mortality has led to the following conclusions.

1. Surgical intervention in the treatment of incomplete abortion has been too frequent and should practically be limited to the control of severe hemorrhage.

2. Prenatal care was freely offered to the mothers of viable children, and more cooperation on the part of the patient might have eliminated a few of the deaths in this group.

3. The infant mortality could be favorably influenced by earlier recognition of some of the underlying causes of stillbirths and neonatal deaths.

4. General hospitals are capable of conducting efficient maternity departments.

from the Ellis Avenue Lying-In Hospital reduces to a ratio only the 35 deaths in the group delivering viable babies. From the standpoint of appraising the efficiency of one's own department in a hospital I am in complete accord with this method. However, from a general census determination it does not alter the irksome fact of a 37 in 10,000 gross ratio in case of the Lying-In Hospital, and a 44 in 10,000 ratio for the Evangelical Hospital. After all as Bolt of Cleveland has pointed out, comparison of maternal mortality rates is misleading unless interpretations of records are comparable. The Memphis vicinity and the Akron, Ohio ratios are mentioned only to emphasize the truth of this statement. Both groups are to be commended on the mass of valuable data brought out by their reports. They lament the high gross mortality rate, but are hopeful that it can be materially reduced by the awakening of "keener interest" among the various agencies concerned in this effort.

Realizing the enormous increase in the number of induced abortions and sensing their damaging influence on gross mortality rates Bolt of Cleveland and Young of London suggest the necessity of separating deaths due to abortions from deaths after the twenty-eighth week of uterogestation if we wish to gain a true picture of the situation. De Lee anticipated this recommendation in the report referred to above by excluding from the gross mortality rate the 13 deaths in 1,334 "sundry obstetric cases." In our series the patients in the abortion group who died had all come to the hospital in critically septic or hemorrhagic conditions for which neither the physician nor the hospital was primarily responsible. All of these patients died of sepsis alone or of sepsis combined with hemorrhage. There were in all 7 deaths from abortions in a total of 390 such cases admitted, a percentage of 1.8 or 180 in 10,000. Abortions therefore cause 28 per cent of the total number of deaths. The method of handling this group is contrary to my personal convictions and practice. Of the 390 abortions of various types 303 received active surgical treatment. Those who died were all septic on admission and are classified as follows: spontaneous 2, criminally induced 2, self-induced 3. Of the 7 patients, 3 were treated conservatively and 4 were curetted. Two of these had been self-induced and 2 were spontaneous.

The 2 deaths in 51 ectopic pregnancies were associated with severe hemorrhage and for some unexplained reason also with sepsis before intervention. The two patients admitted post partum were examples of puerperal sepsis. Both had been delivered at home, one by a physician, the other by a midwife. The undelivered patient who died was operated upon during the sixth month of pregnancy for an intestinal obstruction due to gangrenous volvulus of the small bowel.

The balance of this résumé consists of an analysis of the deliveries of viable babies in the obstetric department proper. This division con-

TABLE I. MATERNAL MORTALITY FACTORS

	MOTHERS	BABIES	TWIN	DELIVERY			CESAREAN SECTIONS	MATERNAL MORTALITY
				NORMAL	FORCEPS	MANUAL		
Total	5,232	5,279	47	4,031	892	273	83	13
Per cent				76	17	5	1.57	0.25
Ratio per 10,000							157	25

In the table it is obvious that certain groups have a higher percentage rate of cures which may be due in part to different criteria for diagnoses of cure. The salts and quinine groups yield comparatively poor results. The halogen-quinoline compounds and picrate radical groups gave quite encouraging results. Huffman used a 6.6 per cent iodochlorhydroxy-quinoline in glycerin and Zenner used the same percentage in an ointment. Janeway's series is small and hence unconvincing.

Karnaky used an organic iodine in glucose. The glucose is to favor the restoration of a normal flora and the iodine compound is to destroy the protozoa and inhibit growth of fungi. This preparation is made up in tablet form. The patient is instructed to place one tablet well up in the vagina night and morning for one week and then one every night for the second week and then one every other night for ten days. The patient should use one tablet every 2 or 3 nights for two or three months as a prophylactic measure. Vinegar douches are prescribed during menstruation. This treatment may be used in pregnancy until the seventh or eighth month. Karnaky had reported prior to this that cornstarch had given moderately good results and at one time advocated "Devegan" highly. He used the organic iodine in the glucose tablet to prohibit a genital mycosis.

The preparation with picric acid and silver picrate gave good results. The picric acid preparations both contained other ingredients which may be important. These were dispensed in suppository form. The silver picrate is used in powder form with kaolin for insufflation and suppository form for home insertion. The patient has 5 gm. of the powder blown or placed in the vagina at weekly office visits. Douches are not permitted. One or two (all these preparations) suppositories are inserted each evening upon retiring, and as improvement takes place the number is gradually decreased. Very infrequently one may encounter an individual susceptible to this salt. It appears that treatment may be needed for three to six weeks. The patient should be examined weekly for a few weeks and then at longer intervals.

Special emphasis is made of the complete failure when arsphenamine, mapharsen, acetarsone, carbarsone, bismuth, and Fowler solution had been used on 25 patients by intravenous, intramuscular or oral routes depending upon the preparation. Sodium arsenate was likewise used upon another 25 patients and these also were not benefited. These data indicate that either these preparations are not especially valuable or that the material does not get to the vagina in sufficient concentration to be potent. Pattyson did not present data establishing why the failure was so consistent.

Except for a moderate flourish of reports about halogen-quinoline substances and silver picrate preparation, the articles about organic arsenical compounds almost entirely dominated this phase of the literature. These preparations are used because of their ability to destroy the trichomonads, but in all instances diluents or vehicles have been utilized. When insufflated, kaolin has been the most common diluent. If suppositories are the vehicle, they have usually been glycerin and gelatin type. The tablet forms have been made up with a carbohydrate. Kaolin and glycerin have each been used more or less alone for this condition and have given some favorable results. Recently the works of Adair and Hessektine, Karnaky, and others have shown that certain carbohydrate

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

VAGINAL TRICHOMONIASIS THERAPY

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CONSIDERABLE confusion must exist in the reader's mind as to the best therapy for vaginal trichomoniasis because of the great number of articles with so many different recommended therapies. This report aims to clear some of the controversial points. Not only have very similar preparations, as the arsenical compounds or the quinine derivatives, been suggested, but an exceptional number of combinations of douches, powders, or tablets are being used. In spite of the many reports, very few controls have been established to evaluate the influence of the vehicles. In many instances one may find contradictory reports by equally good observers on the value of certain preparations.

An analysis of some of the more recent and outstanding articles is undertaken and only these references will be included. Even though some authors failed to clearly state the number of patients treated, a total of 1,650 cases have been subdivided into general groups according to the type of treatment.

The table contains pooled and combined data of representative reports.

The treatment of vaginal trichomoniasis includes douches, medicated by nearly all the antiseptics in current use. Not only have various acid douches been employed by some, but some use sodium bicarbonate and other salts. Until within the last few years many of the treatments consisted of vigorous vaginal scrubbing, even under anesthesia. In the past half decade the popular trend is toward gentle procedures, less frequent office visits and more self-administration by the patient. Considerable microscopic tissue study, chemical determination, bacteriologic classifications of the vagina have indicated certain avenues of approach. At the present time the benefits derived are supposed to come through either the destruction of the trichomonads or the restoration of a normal vaginal flora. It has been shown by many workers that during the reproductive years a cure is associated with the vaginal bacilli predominating almost to the exclusion of the other bacteria and that pus cells completely disappear leaving only epithelial cells. After the menopause the epithelial flora will be nearly the same, but there will not be such a marked preponderance of the vaginal bacilli.

TABLE I. COMBINED AND POOLED DATA FROM REPRESENTATIVE REPORTS OF RECENT LITERATURE

TEST MATERIAL (Trade Name in Parentheses)	APPLICATION	AUTHORS	NUMBER TREATED	PER CENT CURED	ADDITIONAL THERAPY AND REMARKS
Sodium chloride 25%	Douche	Rosenthal, Schwartz and Kaldor	56	86	
Silver salt in ammonia sol.	Douche	Werbatus and Kritschewsky	79	100	Rectal irrigations
Magnesium or copper sulphate	Suppository	Ruble	43	40	Copper used when magnesium failed
			178	81	
Quinine	Insufflation	Kahn	47	100	Sodium perborate douches
Quinine	Insufflation	Sure and Berecy, Pattyson	53	49	
Quinine	Insufflation	Pattyson	37	35	Bladder irrigations
			137	63	
Iodochlorhydroxyquinoline	Instillation	Huffman, Zenner	52	79	
Iodoxyquinolinsulphonic acid (anayodin)	Instillation	Janeway	10	100	
Diiodohydroxyquinoline (floradex)	Tablet insertion	Karnaky	316	100	Douches
			378	97	
Picric acid, menthol and oxyquinoline	Suppository	Mintz	100	95	Douches
Picric acid, formalid, tetraborates and acetanilid	Suppository	Goodall	42	98	Douches
Silver picrate	Insufflation and suppository	Winther, Buxton and Shelanski	120	100	
			262	98	

materials will give about as good a result alone as most of the others. The reports of Bland and Rakoff and Pattysen indicate that there is more value in some protozoacides than with others. Whether these cases were alternately treated and with the materials in use unknown to the one treating the patient was not stated.

Such precautions eliminate some of the human error which otherwise unintentionally enters.

These arsenical preparations are applied at the office by weekly insufflation or tablet insertion. The patient inserts two tablets each evening and gradually decreases their use with improvement as directed by the physician. Douches are forbidden. The patient should return weekly for two to four weeks and then at less frequent intervals as the condition improves. Bland and Rakoff wash the vagina with green soap and water and paint the cervix with tincture of metaphen after which aldarson is blown into the vagina. There is no home treatment. The treatment is daily for three days and then at three-day intervals and then at longer intervals. Gellhorn, in advising stovarsol with kaolin and sodium bicarbonate, suggested treating every other day for two or more weeks. The therapy should be gradually decreased as improvement takes place.

Drabkin has developed a very thorough routine. It requires that the patient take a douche and enema each of soapsuds and then plain water. A carbarsone suppository is inserted into the rectum and 5 gr. each of carbarsone and sodium bicarbonate are dissolved and injected into the vagina and retained. The next morning a suppository is placed in the rectum and in the vagina. This is continued for one week. After the second office visit (eighth day) the treatment is as before except the morning rectal suppository is omitted. From the fourteenth day on, lactic acid or vinegar douches are used in the morning only. Prior to this time acid douches were taken only when necessary for comfort. From the twenty-first day discontinue all rectal therapy but continue to have night vaginal treatment on alternate days. During menstruation take daily acid douches. After forty-eight hours without treatment from the end of the period, the patient is examined and if negative, all treatment is stopped. If positive, the routine is repeated. Unfortunately, this procedure is a bit detailed, yet such thoroughness may be necessary. Drabkin claims good results with this treatment.

Adair and Hesseltine stated that with lactose (95 per cent) and citric acid (5 per cent) they had obtained the best result yet put into practice for their clinic patient. One or two 2 gm. tablets are inserted each evening. Then they are gradually discontinued as the patient improves. Lactose was used as glucose favors a mycosis. Mycoses will very infrequently occur in trichomoniasis cases but only after there has been a partial restoration of the epithelium. In these instances with therapy directed towards the mycosis, which should soon disappear, one may anticipate a very good result. Roblee finds that beta lactose gives excellent results. It is dispensed in large capsules, one of which is inserted once every night or every other night. Whether beta lactose has any more merit than the regular or alpha lactose has not been determined.

Allen and co-workers did an excellent study on the associated urinary tract infections and point out this source of re-infection. Many workers have been convinced that fecal contamination is a very common source for the recurrences. More recently Drummond, Cornell and Riba, Allen,

modo stellarum; coloniis agare dextrose Sabouraudis aestate 20° C. vescentibus densis atque gilvis. Vitulum clarum est, faex abundans. Acetum et bullae oriuntur ex vitulio *dextrose*, *maltose*, *levulose* aut *dextrin*; lac coagulat. Conidia ovata, rotundata, in septis in pseudomyceliis cumulantur, agare farinae zae-maydis, aestate 20° C. vescitur; chlamydosporis rarissimus; leporibus non inuriosa.

SUMMARY

Sixty-eight strains of yeastlike organisms have been isolated from the vaginal tracts of 52 pregnant (32 per cent) and 16 nonpregnant (14 per cent) women.

These strains have been identified and compared with type species of Benham and Stovall by developing a technique which can be carried out in a routine bacteriologic laboratory and which does not require special mycologic training.

The procedures necessary for identification are presented and discussed.

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THE BLOOD PICTURE OF PREGNANCY

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SINCE the turn of the century, a tremendous volume of literature has accumulated on the subject of anemia of pregnancy. A résumé of this indicates that a small percentage of women may develop either an hypochromic or pernicious anemia, that a larger group do not deviate from normal, and that a still larger group have a lowering of hemoglobin and red blood cells not of the type that can be classified with the anemias mentioned. It is this latter group of women in whom the controversy arises, whether the change in the blood is physiologic or pathologic. Most authors concede that there is a physiologic change, but there is no concurrence of opinion as to its extent. Sporadic outbursts of enthusiasm for methods of treatment are futile until we settle in our own minds within what limits the blood may normally vary, and what is more important, create a better knowledge of hematology in pregnancy. We prefer the term "blood picture" of pregnancy, to "anemia," in this discussion.

TABLE I—CONT'D

Neostephamine, napharsen, bismuth, Fowler's solution, acetarsone, carbarsone, sodium arsenate	Oral and in- tracutaneous	Pattysen	50	None
			50	
Acetarsone (stovarsol)	Insufflation	Gellhorn	No number given—excellent results	
Acetarsone	Insufflation	Bland and Rakoff, Pattysen	52	52
Acetarsone	Insufflation	Pattysen	37	70
Cinquarsin (7½ gr. and 1½ gr. salicylic acid)	Insufflation	Goldstein	No number given—excellent results	Bladder irrigations
Cinquarsin	Insufflation	Pattysen	25	84
Cinquarsin	Insufflation	Pattysen	55	96
Paroxyl (devegan)	Tablet insertion	Koelsch and Tsutsu- lopulos, Fuge	220	99.5
Carbarsone	Suppository	Gospe, Drabkin	72	78
Aldersone	Insufflation	Bland and Rakoff	100	91
			561	88
Lactose with citric acid (no drug)	Tablet insertion	Adair and Hesselstine	66	91
Lactose (beta)	Capsule insertion	Roblee	No number given—excellent results	Treat foci
			Total 1650+	86

Jensen and Wood, Karnaky, Adair and Hesseltine, and others have obtained evidence that the male can be a direct source of infection or re-infection.

Consequently, it is not only necessary to cure the patient and restore the vagina to its normal state but necessary to prevent all re-infections. The urethra and bladder of the female may need treatment. Some controversy exists yet whether the vaginal trichomonads may or may not be harbored in the intestine. Because there have been few well-observed instances in which an exacerbation of vaginal trichomoniasis followed the contact of the vulva with feces, one should treat the intestinal tract or at least instruct the patient about anal hygiene.

If the patient does not respond properly or has recurrence, the husband should have an examination by a competent urologist. Some workers have insisted that every husband have this examination.

Perhaps as time goes on other sources may be discovered. One thing is well established and that is with the restoration of the vagina to a normal cellular and bacteriologic flora the disease entity vanishes.

Moreover, it is urged that before any new procedures or preparations be recommended adequate and satisfactory controls be established, because the milder cases and the new ones often respond nicely to so many procedures. The test is best evaluated by the results obtained in old chronic cases or severe resistant infections.

Cures should not be diagnosed until the patient has gone through at least two complete menstrual cycles without treatment, remains free from symptoms, appears clinically normal, and has no microscopic evidence of the protozoa or infection. These examinations are advisable a few days after menstruation ceases. The obstetric patient, although apparently cured toward the end of pregnancy, should be examined postpartum. The postmenopausal patient must be observed for over two months under the same condition as above and examined at least two or more times during this interval. Perhaps a longer period of observation may be indicated with more frequent tests.

With whatever method one uses his best results occur only when it is carried out completely and enthusiastically without omission of any small details, and yet with the persistence to get the best possible results. Moreover, the recent reports by various workers indicate the real value of preventing recurrences. The patient's own urethra and bladder or possibly rectum are sources. Hence, one should particularly advise the patient about anal hygiene. If improvement fails or recurrences arise, a thorough investigation of the urethra and bladder is indicated. Even the husband should have an urologic examination by a competent urologist if his wife fails to respond to treatment or remain free from the disease.

Let it be remembered that the two phases of therapy are (1) curative and (2) prophylactic. The former means to cure the patient, while the latter means the prevention of new infection during the treatment period or following cures.

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NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 11, 1937

The following papers and discussions were presented:

A Clinical Evaluation of Stereoroentgenography of the Female Pelvis. Drs. Kyle B. Steele, Lucius A. Wing and Charles M. McLane. (For original article, see page 938.)

Pelvicephalometry—a Volumetric Ratio Between the Pelvic Diameters and Fetal Cranium. Dr. Robert P. Ball.

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 21, 1937

The following papers and discussions were presented:

Maternal and Fetal Mortality in a General Hospital Where the Majority of the Obstetric Work is Being Done by the General Practitioner. Dr. Paul C. Fox. (For original article, see page 1074.)

Analysis of Obstetric Material of the Evangelical Hospital of Chicago. Dr. Christian D. Hauch. (For original article, see page 1081.)

Masculinizing Elements in the Ovary. Dr. Ralph A. Reis, and Otto Saphir. (For original article, see page 954.)

Blood Chemistry Observations in Protein Deficient and Toxic Pregnancies. Dr. M. Herbert Barker. (For original article, see page 949.)

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 1, 1937

The following papers and case reports were presented:

Carcinoma of the Breast and Pregnancy. Dr. Alex. H. Rosenthal (by invitation).

Alexander J. C. Skene. Dr. T. S. Welton.

Review of 24 Cases of Hydatidiform Mole with Follow-up. Dr. M. V. Armstrong.

Syphilis in Pregnancy. Dr. W. T. Daily.

Pelvic Tuberculosis. Dr. J. V. Cresci and Dr. M. Glass.

X-Ray Diagnosis of Placenta Previa. Dr. A. C. Beck and Dr. F. P. Light. (For original article, see page 1028.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Gonorrhea

Antoine, T.: *Gonorrhea in the Female*, Wien. klin. Wchnschr. 28: 883, 1936.

The gonococcus is not only a mucous membrane parasite; it also invades the sub-epithelial tissues, uterine musculature and parametrium. Gonorrhea in the acute form in the female is rarely seen by the physician. For diagnosis and differential diagnosis, smears and complement fixation tests are necessary.

In acute cases rest in bed and warm Sitz baths together with dilute KMnO_4 irrigations serve very well. In cases of urethritis and cystitis disinfection of the urine with urotropin and salol is all that is necessary. After the acute stage, instillations of AgNO_3 -1 per cent or colloidal silver may be used in the urethra; the urethral glands may be treated by endoscopy. In involvement of Skene's and Bartholinian glands, instillation of 5 per cent to 10 per cent AgNO_3 may be made with a cannula. With involvement of the latter glands, conservative treatment usually suffices; if this fails and an abscess forms incision and drainage is the treatment of choice. These are usually mixed infections. Condylomata acuminata are specific infections of another nature; these may be treated by Sitz baths, surgical excision or diathermy. Colpitis gonorrhoeica in children and old women may be treated with 1 per cent to 5 per cent AgNO_3 , 5 per cent protargol or with follicle hormone. Cervicitis is difficult to treat; protargol-glycerin tampons may be applied to the portio. In chronic cervicitis intractable to treatment, the Sturmdorf operation may be done. During pregnancy treatment should be limited to the cervix and urethra and should be discontinued within 14 days of delivery. No treatment is given in the early puerperium; precautions must be taken to prevent ascending infection.

In addition to local treatment there are 3 forms of general treatment: heat, fever therapy, and vaccines. In the subacute stage, heat may be applied in the form of air, lamp, diathermy or hot packs. Fever therapy is carried out with protein substances, dyes, metallic colloids, iodine and turpentine preparations. Vaccine therapy should be used only in selected cases with deep seated infection. In cases of ascending infection, conservative and symptomatic treatment should be carried out; pain may be relieved with analgesics, viz: pyramidon, antipyrine, and only occasionally morphine or pantopon. With conservative management excellent results are obtained but complete anatomic restitution is uncertain. In those patients who do not make a perfect recovery after long conservative management, surgical interference may be necessary. It must be radical with removal of uterus and tubes or fundus and tubes at least. As for cure, all smears must be negative and smears following provocative coitus condomatus must also be negative.

W. B. SERBIN.

Brunet, Walter M., and Salberg, Joseph B.: *Gonorrhea in the Female*, Am. J. Syph. Gonor. & Ven. Dis. 21: 64, 1937.

In the authors' experience pelvic extensions in gonococcus infection are usually delayed until the second, third, or even fourth menstrual epoch, but in this series, 26 of the 30 instances occurred between thirty or forty days. There is no doubt in their mind that the cause for these precipitate complications was directly attributable to

the treatment employed. There is no known method by which the actual cause for these distressing complications can be demonstrated, but it is their conviction that neisso-jel (gonophage) in some unknown manner altered the local tissue response and thereby contributed to an upward dissemination.

Pelvic complications occurred early. The clinical symptoms pointed toward a severe peritoneal irritation rather than a true adnexitis. The pelvic findings were not comparable with the intensity of the local symptoms. Extension of the infection to the pelvic organs occurred in 32 of the 88 patients. The use of gonophage preparations in the treatment of gonorrhea in the male has been disappointing when injected even in small doses or applied topically, and systemic reactions have occurred.

C. O. MALAND.

Zoeltsch-Lass: The Frequency of Occurrence and Treatment of Gonorrheal Bartholinitis, München. med. Wehnsehr. 84: 210, 1937.

Out of 150 cases of gonorrhea 34 had a Bartholinitis; 10 of them on the right side, 10 on the left and 12 bilateral, and in the remaining two instances the abscesses were sterile on culture. Ten of the cases were associated with urethral and cervical gonorrhea. Treatment followed four main methods: electrocoagulation, electrocoagulation together with the use of 10 per cent silver nitrate, injection with 2 per cent silver nitrate and the use of compligon (a sulfanilamide preparation) and 2 per cent silver nitrate. Cases of simple Bartholinitis respond to oral prontosil and electrocoagulation, or the injection of 2 per cent of silver nitrate.

J. P. GREENHILL.

Brunet, Walter M., and Salberg, J. D.: Gonococcus Infection of the Anus and Rectum in Women. Am. J. of Syph. Gonor. & Ven. Dis. 20: 37, 1936.

Gonorrhea of the anus and rectum occurred as a complication in 38 per cent of 250 cases of gonococcal urethritis and cervicitis. The mode of invasion is presumably through direct contamination by the vaginal and urethral secretions and the incorrect use of toilet paper. The symptoms of rectal gonorrhea are usually mild and are often entirely absent. Chronic gonococcal infection of the rectum may act as a focus of reinfection of the urethra and cervix.

Complications of rectal infections, such as abscess, fistula, and ulceration, are infrequent. In four patients a perineal abscess developed and three patients had rectal fistula. Repeated examination of rectal slides should be carried out as a part of the routine in all women suspected of gonorrhea. The treatment of gonorrhea of the anus and rectum should be conservative. Instrumentation which causes pain and the use of irrigations should be avoided. In 59 patients examined after intervals of six months to two years, 10 were found to be positive for gonococci.

C. O. MALAND.

MacLennan, Jean M.: Gonococcal Arthritis in the Mother and Newborn Infant, Brit. M. J. 2: 121, 1936.

Gonococcal arthritis in pregnancy and the puerperium is a commonly recognized condition. Gonococcal arthritis in the newborn infant is less common. The coincidence of the two is rare. A case of arthritis complicating gonococcal ophthalmia neonatorum is described. Gonococcal arthritis was present in the mother. The literature is briefly mentioned. The joint affected in the infant was the left thumb, a rarely attacked joint in ophthalmia neonatorum. In this case the early rupture of the membranes during labor probably accounts for the infection of the eyes. The mother's complement fixation reaction was strongly positive, while that of the infant was negative when the arthritis was at its height. Later it became weakly positive. Is there any analogy here to the negative Wassermann reaction obtained in some very young infants whose blood is found two or three months later to be positive?

F. L. ADAIR AND S. A. PEARL.

Spohr, Carl L., and Landy, Maurice: A Cultural Method for the Diagnosis of Gonorrhea Employing the Direct Oxydase Reaction, *J. Lab. & Clin. Med.* 21: 650, 1936.

Satisfactory results have been reported for the diagnosis of gonorrhea by cultural methods. McLeod and his associates first introduced the use of the direct oxydase reaction for the detection of gonococcal colonies in mixed cultures. Spohr and Landy applied this reaction to routine laboratory use.

Of 59 patients examined, positive cultures were obtained in all cases showing positive urethral smears and in 6 cases showing negative urethral smears. With reference to the cervix in chronic cases the smears were positive in 18.6 per cent and the cultures positive in 50.8 per cent. The oxydase reaction is not specific for the gonococcus; false positive reactions may be given by *B. coli* and *B. subtilis*, but these organisms are easily distinguishable from gonococci, both microscopically and macroscopically. In addition, Thompson of the Mayo Clinic, reports a positive oxydase reaction with *Neisseria catarrhalis*, *Neisseria flava*, and *Hemophilus influenza*. These results emphasize the absolute necessity of a microscopic examination of oxydase positive colonies in all cases.

W. B. SERBIN.

Cohn, Alfred: The Importance of Bacteriologic Cultures for the Diagnosis of Gonococcal Vulvovaginitis and Proctitis in Children, *Am. J. Syph. Gonor. & Ven. Dis.* 20: 623, 1936.

A new modification of Levinthal's blood-extract agar and a simplified technic for testing fermentation reactions of gram-negative diplococci are described. In collaboration with Bayne-Jones, the procedure has been considerably simplified without impairing the useful qualities of this medium. The results obtained by this method indicated clearly that reliable etiologic diagnosis can be made only by means of bacteriologic cultures, and evidence is presented which warrants the conclusion that cultures for gonococci should be made routinely in cases of vulvovaginitis and proctitis in children.

C. O. MALAND.

Cohn, A.: The Gonococcus Complement Fixation Test, *J. Lab. & Clin. Med.* 22: 627, 1937.

With the discovery of the gonococcus, the difficulty in diagnosing cases of subacute and chronic gonorrhea was further emphasized. In some series reported, gonococci were demonstrated in females in 40 per cent of chronic cases after an examination of seven smears; in other series it has been possible to demonstrate these same organisms only after an examination of 70 to 80 smears. With the adoption of the culture method, there seemed to be some increase in the efficiency of diagnosis of gonorrhea. Even these laboratory procedures are limited, particularly in the cases in which gonococci have penetrated deeply into the tissues so as to disappear completely from the discharge. This type of latent gonococcal infection is a frequent complication of the disease in the female sex organs. As smears and cultural procedures are not always of value in the diagnosis of latent gonorrhea, the complement fixation test becomes a particularly useful aid for diagnosis. The main difficulty in the past has been the lack of a suitable antigen for the test. Attempts to improve these reagents are constantly being made. Blood is drawn just as for a Wassermann test and reactions are designated as 1-plus to 4-plus. Material obtained from various types of patients was used in this series. Tests were done on 495 patients but of special interest are 271 adult females and 25 children of whom 24 were females. Not all of these patients had clinical gonorrhea and tests thus were made to clear up obscure disorders. There were 30 cases of cervicitis, 18 cases of adnexitis and 4 cases of Bartholinitis.

In the group of cases with cervicitis, 7 had a 4-plus, 5 a 3-plus and 5 a one or 2-plus reaction. In the group with adnexitis, 11 had 4-plus, 2 a 3-plus, and 4 had a 1- or 2-plus reaction. In the group with Bartholinitis, 1 had a 4-plus and 3 a 1-

or 2-plus reaction. The author describes his technic of the complement fixation test for gonorrhea. He concludes that the production of complement fixing antibodies is dependent on the duration and spread of the infection. In acute complicated cases, the complement fixation test is strongly positive; in chronic cases the reaction is sometimes only weakly positive. This test is an aid in the determination of cure if previously positive reactions become negative, and the clinical and bacteriologic findings are also negative. A negative reaction by itself does not mean absence of gonococci. A positive reaction, persisting longer than one year after a clinical and bacteriologic cure, is an indication of a latent focus. This test is not intended to replace the older known methods of diagnosis but should be a supplementary procedure helpful in the diagnosis and in determination of a cure.

W. B. SERBIN.

Lewis, R. M., and Adler, E. L.: **Gonorrheal Vaginitis in Children**, *Am. J. Surg.* 33: 529, 1936.

The only treatment given consisted of intravaginal insertion of a suppository containing 1,000 I.U. of amniotin each night at bedtime. The use of the suppositories was continued for at least two weeks after the vaginal discharge had ceased and the smears were negative. The external genitalia were washed when necessary. This therapy was continued until now 48 cases have completed their treatment and have been free from discharge and show negative smears for periods from three weeks to eleven months. On an average the smears in this series became consistently negative after 24.5 days of treatment.

It is significant that the hospital stay of cases treated in 1933 was 185 days and the cost to the city approximately \$400.00 for each case. Moreover, during that year under the older methods of treatment only 82 were discharged from a total of 185 cases. The saving of time to the patient and expense to the city would seem to be considerable.

J. P. GREENHILL.

Pongratz, R.: **The Hormone Treatment of Gonorrheal Vulvovaginitis**, *Med. Klinik.* 33: 93, 1937.

The author employed estrogenic hormones in the treatment of four children who had gonorrheal vulvovaginitis. In all four cases, negative smears were obtained after two weeks of treatment. In all, the vaginal discharge disappeared rapidly. No disturbances were observed such as swelling of the breasts or increased hair growth on the pubis.

J. P. GREENHILL.

Di Paola, G.: **Treatment of Gonorrheal Vulvo Vaginitis in Children With Follicular Hormone**, *Bol. Soc. Obst. y ginec. de Buenos Aires* 16: 242, 1937.

The author reports the use of Progynon in the treatment of nine cases of gonorrheal vulvovaginitis in children. Good results were obtained with eight of the patients over a period of two months.

MARIO A. CASTALLO.

Bierman, William: **Treatment of Gonorrhea in Women by Means of Systemic and Additional Pelvic Heating**, *New England J. Med.* 218: 60, 1938.

Particularly good results in the treatment of gonorrheal infections are claimed for a combination of systemic raising of temperature with differentially increased pelvic heating. Body temperature is elevated by photothermal and shortwave heating with patient lying in bed or in hot water bath. After general body temperature has reached 106° F. locally in the pelvis the temperature is raised to 108° or 110° F. by special shortwave apparatus. Details of the technique are given. Of 125 patients, definitely infected with the gonococcus, in 93 per cent the gonococci disappeared.

HUGO EHRENFEST.

Dees, John E., and Colston, J. A. C.: Sulfanilamide in Gonococcic Infections, J. A. M. A. 108: 1855, 1937.

Nineteen cases of gonococcic infection were treated with sulfanilamide. Of these, the active urethral discharge disappeared in three cases in one day, in seven cases in two days, in two cases in three days, in two cases in seven days. In one case it disappeared in four days to recur slightly on the fourteenth day and again disappeared on the sixteenth day. In two cases the discharge is still present ten and twelve days after the beginning of the treatment. Stained smears from the urethral discharge and centrifuged urine became negative for gonococci in five cases in two days, in five cases in three days, in two cases in five days, and in one case each in four, six and twenty-three days.

With a few exceptions, all patients received, in four divided doses a day, a total of 4.8 gm. of sulfanilamide daily for two days, 3.6 gm. daily for three days, and then 2.4 gm. daily for from four to eight days. No other treatment, local or general was used. Fluids were not forced, as it was thought that this would hasten the elimination of the drug. Alcohol and sexual activity were prohibited.

The use of sulfanilamide in gonococcic infections is as yet in the experimental stage. Yet, the prompt response to treatment in the vast majority of cases has impressed the writers greatly.

GROVER LIESE.

Items

American Board of Obstetrics and Gynecology

The oral, clinical, and pathological examinations for Group A and Group B applicants will be held in San Francisco, California, on Monday and Tuesday, June 13 and 14, 1938.

An informal dinner for the Diplomates of this Board, their wives and others interested in the work of the Board, will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, will address the group, and the successful candidates of the preceding two days' examinations will be introduced in person. Tickets, at \$2.25 each, may be obtained in advance from Dr. Joseph L. Baer, 104 S. Michigan Avenue, Chicago, Illinois, or at the door. Reservations should be made in advance if possible.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

Dr. Geo. Gray Ward of New York has been made a Foreign Corresponding Member of the Royal Medical Society of Buda-Pesth, on the occasion of the Commemoration of the one hundredth anniversary of the founding of the organization.

Dr. Oskar Frankl, of Vienna, an Honorary Fellow of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, well-known gynecologist and teacher, died recently in his home city.

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What are some of the factors which may influence the blood picture of pregnancy? The preexisting state of the patient's blood, a diet lacking in the necessary materials for blood formation, changes in the gastrointestinal tract depressing assimilation must be considered. Even more interesting is the effect of the creation of a new, highly vascular organ, the pregnant uterus, on the existing circulation, the fluid changes in the blood stream and tissues, fetal demands, the possibility of increased hemolysis, and the influence of altered glandular function on the hematopoietic system. Some of these factors we may be able to control but others we cannot, nor would we be justified in considering them as needing control. If it is granted that during pregnancy there are influences acting to alter the usual blood picture, we must endeavor to evaluate each one before accepting as fact that lowered hemoglobin and red cell count must mean anemia.

We feel that there should be acceptance of the evidence showing increase in the water content of the blood plasma during pregnancy. Several investigators have presented evidence to prove this change, of whom we would like to mention two.

The work of Van Donk and associates¹ is of considerable interest. Experimenting with rats, they found a consistent "anemia" during pregnancy which was not influenced by forced feeding of high protein, iron, and vitamin content diets and upon studying the fluid changes occurring in the blood, came to the conclusion that increased water content was the cause of the apparent anemia, suggesting this as the probable cause of the same phenomenon in human beings. Oberst and Plass² in a recent publication have shown the same fluid changes in the blood plasma of pregnant women. While the degree of the increased water content of the plasma is subject to variation in different individuals, there can be but little doubt that this factor is a major one to explain the lowering of blood values in pregnancy. Hemoglobin and red blood cell levels may be even more markedly lowered by "watering" of the plasma than has been stressed.

Many investigators have made the observation that the "clinic" patient has a lower blood level than the "private" patient and have advanced this as evidence of the adverse effect of improper diet and environment. That diet is a considerable factor cannot be denied, the outstanding example of which is the 3 per cent hospital incidence of pernicious anemia of pregnancy among the women of India, described by Wills,^{3, 4} which she has shown to be dietary in origin, particularly referable to long-standing vitamin B deficiency. However, diet can be overstressed and used as a cloak under which to hide our faulty understanding. Nutritional anemia among all classes of patients, exclusive of pregnant women, is of relatively infrequent occurrence in clinic or private practice in this country. By the term nutritional anemia, we mean an anemia based entirely on food ingested and not disorders of assimilation. Why should the pregnant woman, stimulated as she is by pregnancy and usually tending to overeat, be peculiarly susceptible to nutritional

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anemia? The influence of diet and environment seems of relatively less importance than the effect of pregnancy per se on the blood picture.

Despite all that has been published, we do not feel that the blood picture of pregnancy has been investigated to the fullest extent. We have made an effort to intensively study our patients not only during pregnancy but for a considerable period thereafter. Our results are at variance with many published and as a consequence, the conclusions differ radically from those generally accepted. That you accept these conclusions is not of as much importance as that the present knowledge of anemia of pregnancy be considered with a healthy skepticism.

METHOD

Our object was to establish data on a sufficiently large group of pregnant women to determine in general their percentage distribution in regard to hemoglobin level both antepartum and postpartum as a basis of discussion. Our next step was to make an intensive study of a smaller group of women, selected from those adjudged anemic by current standards in order to elucidate some of the factors we have previously mentioned as contributing to the blood picture of pregnancy.

The first group mentioned above comprises all confinements in the University hospital during a one-year period, 500 in number. These patients had one or two hemoglobin determinations antepartum and a like number during the postpartum hospital period.

The second group of women, 50 in number, were selected from patients who at the first clinic visit had hemoglobins of less than 70 per cent Sahli. Each patient of this group was instructed to report every two weeks for a hemoglobin determination and red blood cell count. Capillary blood was used at one visit and intravenous blood at alternate visits, the latter for hematocrit readings and blood counts. Gastric analysis was done when the patient would consent. The gastric analysis was of the routine type, using the alcohol test meal, and when no free hydrochloric acid was found, histamine injections were given. Gastric analyses were done as early as possible during pregnancy. A three-day diet record was obtained from the majority of patients, this being in the form of an itemized account of all food eaten during this period as well as the amount. All patients were instructed to take no medication during the period they were under observation and this request was adhered to in every instance. Four patients were treated; these will be mentioned later.

The study was continued throughout the pregnancy and for as long as fifteen months postpartum. Since relatively few of the obstetric patients enter the clinic during the first trimester, our observations did not include this period as a rule. On the tenth postpartum day, while the patient was still in the hospital, an intravenous blood specimen was taken for hematocrit reading and a blood count. We endeavored to have patients return when six weeks postpartum and thereafter at frequent intervals for as long as fifteen months. No effort was made to select patients according to parity, but since the majority of the women attending the clinic are primiparous, primiparas form the largest number in the group.

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 treatment of, in children with follicular hormone (Di Paola), 1095 (Abst.)
 mycotic or diabetic (Hesseltine and Campbell), 272

W

Weight changes in pregnancy (Bray), 802
 Wheat germ oil therapy (Shute), 249, 609, 810
 vitamin E (Watson), 922 (Abst.)
 treatment of habitual abortion with (Vogt-Moeller), 923 (Abst.)
 Woman's life, intimate side of (Chalmers), 353 (B. Rev.)

X

X-ray diagnosis of placenta previa (Beck and Light), 1028
 in diagnosis, dermoid cyst of ovary in child five years old, with comments on value of (Mazzola and Ryan), 696

Y

Yeastlike organisms, identification of, isolated from vaginal tracts of pregnant and nonpregnant women (Jones and Martin), 98

A point of peculiar significance to be noted in Chart I is the rather sudden return of the blood to higher levels in the immediate postpartum period. When it is considered that a number of these women had abnormal blood losses at the time of delivery, the phenomenon becomes more remarkable. If the fall of hemoglobin during pregnancy were true anemia, the shift toward normal would be difficult to explain. Instead of an immediate decrease in the number of patients with less than 55 per cent hemoglobin, at least a temporary increase would be expected. One would not look for a favorable reaction from blood loss in the presence, for instance, of a gastric ulcer associated with an anemia, yet the blood loss incidental to delivery does not have the predicted effect

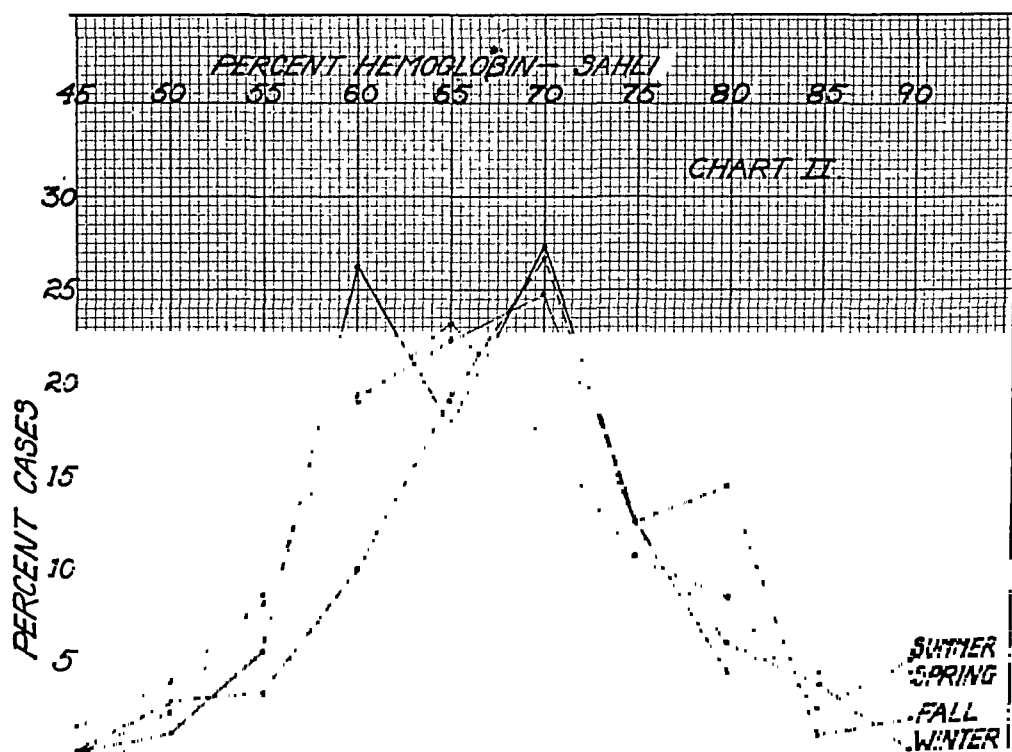


Chart II.

were we dealing with an anemia. The physiologic factors, particularly hydremia, seem to us to become most evident in the explanation of the postpartum reaction of the blood.

Diet and environment as a factor in the blood picture of pregnancy do play their part, but to what degree they cause significant lowering of blood levels is difficult to estimate. Chart II represents the group of 500 pregnancies, segregated into the seasons during which the original hemoglobin and red cell counts were made, in accordance with their percentage distribution based on the hemoglobin. No seasonal variation is apparent, and from this we infer that the variation in available food and sunshine is not of sufficient significance to be reflected in the blood picture of these women. Two-thirds of the selected group of patients

collected for hematocrit reading were diluted with 1.4 per cent potassium oxalate solution as the anticoagulant. The laboratory work was done in the Hematological Laboratory of the University clinic by a single, trained technician.

DATA AND DISCUSSION

We wish to discuss first the results of the investigation of the group of 500 women. Chart I illustrates the percentage distribution of this group based on hemoglobin values. The majority, 81 per cent, had hemoglobin values of between 55 and 75 per cent Sahli during the antenatal period. That 81 per cent had hemoglobin values as shown seems conclusive evidence of the magnitude of the downward trend of blood levels during pregnancy. Adair, Dieckmann, and Grant⁵ in their recent paper on

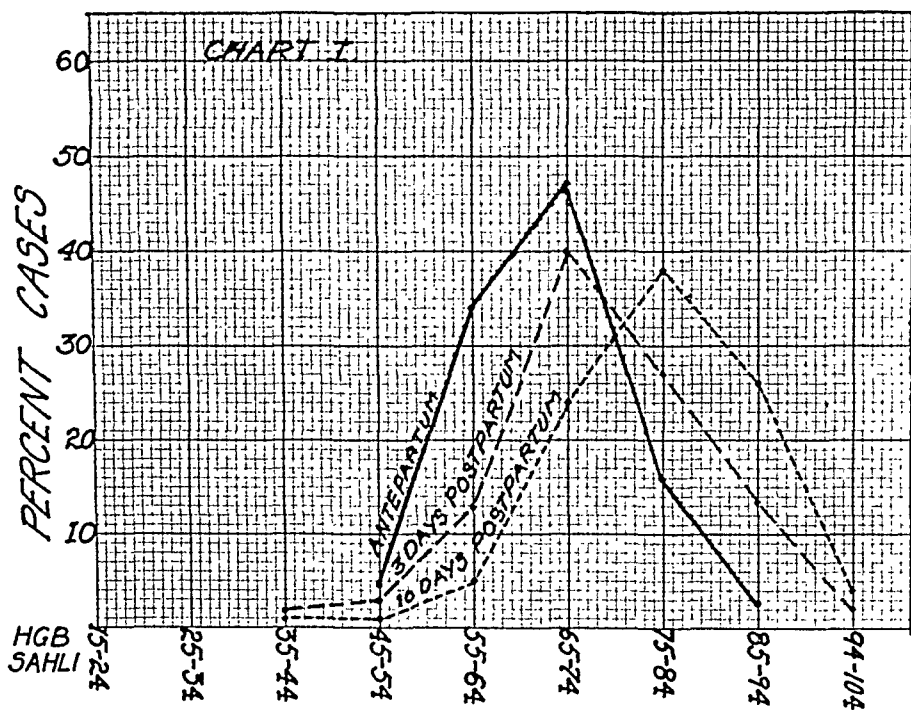


Chart I.

anemia in pregnancy, state that 63.2 per cent of 7,800 women studied had an anemia according to the standards for the nonpregnant, and 11.6 per cent were truly anemic when the standards which they adopted for pregnancy were used. Comparing their statistics to ours, in general there is agreement, but their series shows a greater number of women with better than 70 per cent hemoglobin. Both studies show a preponderance of women with hemoglobin below 80 per cent—63.2 per cent in theirs, 81 per cent in ours. The lower limit of normal for hemoglobin in pregnancy must of necessity be arbitrarily set due to the fundamental lack of knowledge. As a result of the study of a selected group of patients to be discussed later, we place the lower limit of normal at 55 or 60 per cent Sahli. Referring to Chart I again, roughly 5 per cent of our patients had hemoglobins of less than 55 per cent Sahli, which we feel is the probable incidence of true anemia during pregnancy.

the antenatal period. This was true of a few, but in only one case was the drop as term approached appreciable. The exception was a patient who had an exacerbation of a chronic pyelitis during her pregnancy. The hemoglobin dropped to 50 per cent at term, but one month postpartum without treatment was 80 per cent. If the drop in blood level is pathologic, the maximum fall in hemoglobin should coincide with the maximum development of the products of conception. Studies by Coons⁶ have shown that the demands of the fetus for iron are increasingly greater as term is approached. Our data do not demonstrate the relationship between the mother's hemoglobin and the changing fetal requirements.

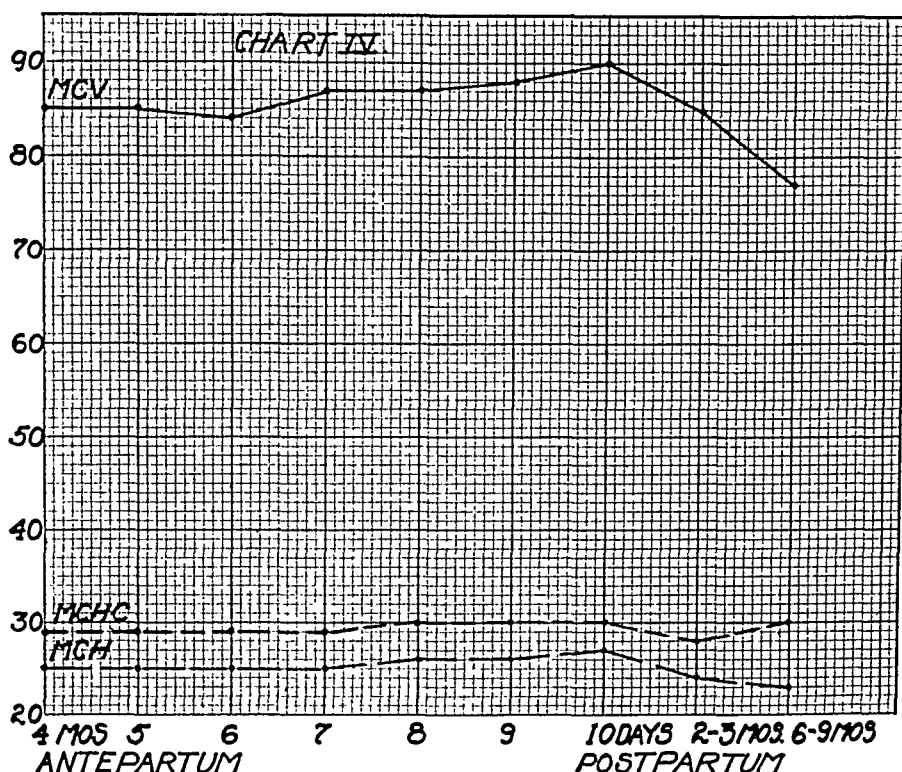


Chart IV.

In a relatively large percentage of the group, a spectacular rise of the hemoglobin to normal was noted in the last trimester. A precipitous rise of the hemoglobin from 55 or 60 per cent to 90 per cent or over dispelled any idea that we were dealing with an anemia. We noted that those patients whose hemoglobin rose to 90 per cent or over before delivery maintained that level postpartum, whereas those whose level at term was below 80 per cent, would, after delivery and as much as fifteen months postpartum, not develop more above 80 per cent. From this we advance the idea that there are in general two groups of patients to be considered, those who in the nonpregnant state have high normal hemoglobin and those who have low. Obviously, if a woman normally has 95 per cent hemoglobin and drops to 70 per cent during pregnancy, then

submitted three-day diet lists, and a study of these showed a moderately well balanced diet, not lacking in the essential foodstuffs. While the patients favored carbohydrate in their diet, there was no evidence to show a protein deficiency. Those women having the lowest average hemoglobin during pregnancy had diets indistinguishable from others with higher hemoglobin. We think that only the extremes of poverty, adverse living conditions and perversity of appetite are appreciably reflected in the blood picture of pregnancy.

Our discussion now turns to the group of 50 patients selected for special study and observation of the blood uninfluenced by treatment. Of the 50 women, 10 have been excluded as the basis of data for charts;

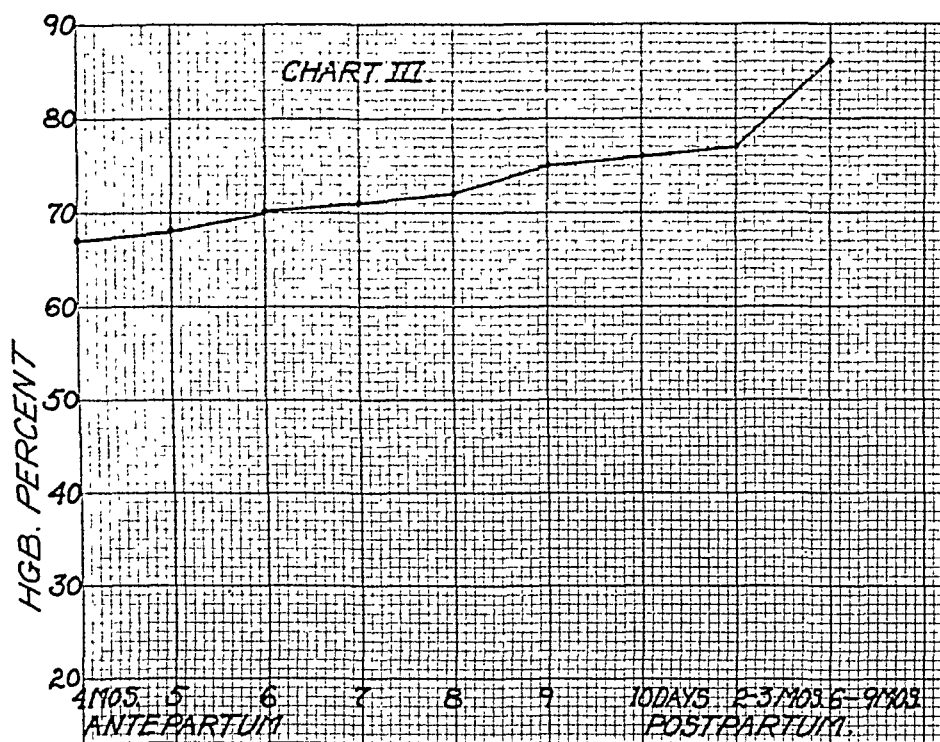


Chart III.

4 because they were given treatment, 2 having hypochromic anemia, 1 the blood picture of pernicious anemia, and a fourth, who was treated in error. The other 6 were excluded because only the first hemoglobin was less than 70 per cent.

Chart III represents the average hemoglobin reading of this group of women antepartum and postpartum. From the fourth month on, a steady upward climb of the hemoglobin level is noted, being at term only slightly less than normal (77 per cent). At six to nine months postpartum a normal level is reached, but even at ten days postpartum the hemoglobin is practically normal. When it is considered that these women were selected because of hemoglobin below the accepted lower limit of normal for pregnancy, the chart is unusual. One might expect that in this group there were those whose hemoglobin did not rise during

In the study of the gastric analyses performed upon 24 of the women, it was hoped that the factor of faulty food assimilation due to altered gastric secretion might be demonstrated. In Chart V, the lower graph represents the total acidity of the four specimens of each patient. The upper graph shows the average of all hemoglobin readings for the same patient throughout the antepartum period. A total free hydrochloric acid content in four specimens of 100 has been taken as the lower limit of normal. Four patients were normal and a similar number had an achlorhydria; 73.4 per cent of the series had a low hydrochloric acid secretion. The striking similarity of results published by Strauss⁸ who studied a similar number of women, reporting 75 per cent with less than normal hydrochloric acid secretion during pregnancy, is worthy of mention. An effort to correlate the average hemoglobin reading and the gastric acidity of each patient resulted in a correlation coefficient of 0.42, too low to prove a direct relationship. Gastric analysis did not prove a diagnostic aid in predicting the course of the hemoglobin level during pregnancy. Further efforts to prove a relation between altered assimilation of food during pregnancy and its bearing on the blood picture will require more detailed study of gastric secretion than is obtained by this procedure.

Routine estimations of the icteric index were made from the hematocrit specimens. The readings were from 2 to 7.5; two patients had icteric indices as high as 10 on one occasion. Since the icteric index did not tend to deviate from normal, we cannot say from this laboratory procedure that there is evidence of increased hemolysis during pregnancy.

While we think that it is possible for the hemoglobin to drop to 55 per cent during pregnancy and represent a purely physiologic change, we do feel that any patient with less than 60 per cent hemoglobin should be investigated and an hypochromic or other type of anemia ruled out. Our experience is that specific anemias will usually result in a hemoglobin of less than 55 per cent early in pregnancy, certainly by the fourth month.

CONCLUSIONS

1. The majority of pregnant women have a lowered hemoglobin and red blood cell count which is physiologic and its extent influenced by the hemoglobin level in the nonpregnant state.

2. The physiologic lowering of the hemoglobin during pregnancy may reach 55 per cent Sahli (7.7 gm. hemoglobin per 100 c.c.).

3. Patients with true anemia will present the picture relatively early, certainly in the first half of pregnancy.

4. The magnitude of the problem of anemia of pregnancy is not as great as that generally stated, and probably is in the neighborhood of 5 per cent.

one whose hemoglobin is 80 per cent might be expected to drop to a variable degree below 70 per cent, since the same factors are operating in each case. It is interesting to note that none of the patients were anemic six to nine months postpartum. Two had given histories of anemia antedating their pregnancy, but neither of these women proved to be so during the many months they were observed after delivery. We can safely state that pre-existing anemia was not a factor in the blood picture of these women during pregnancy, if the resumption of normal hemoglobin after delivery is accepted as evidence of their usual hemoglobin level.

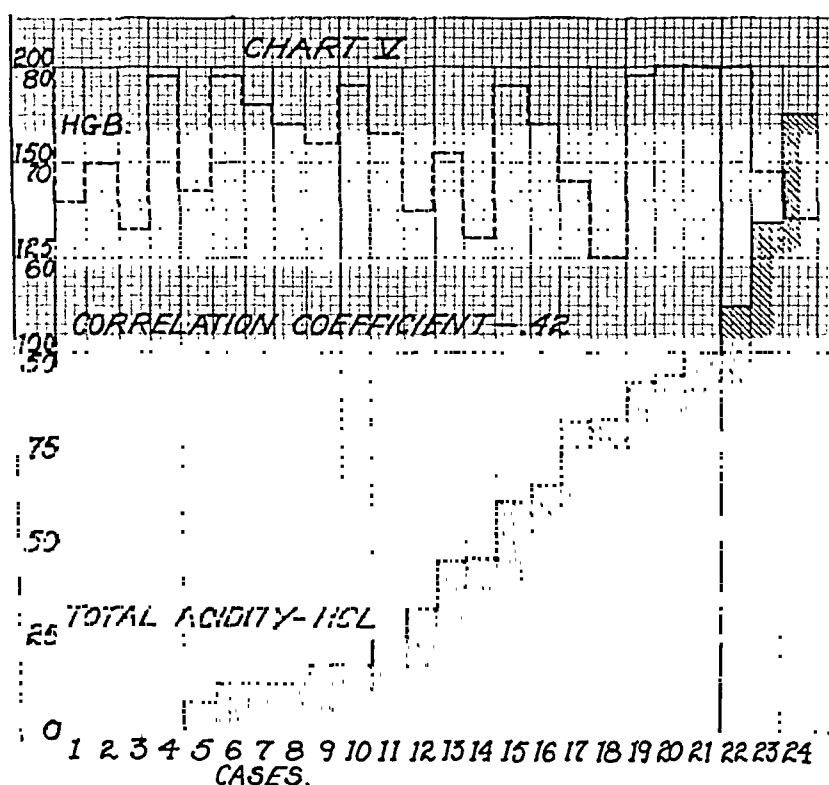


Chart V.

Consideration of the hematocrit readings reveals an interesting point. As shown in Chart IV, which gives the average mean corpuscular hemoglobin, corpuscular volume and corpuscular hemoglobin concentration, antepartum and postpartum, of 40 cases, the general level of the calculations falls within the normocytic range of Wintrobe.⁷ Six to nine months postpartum, despite the return of the hemoglobin and red cell count to normal, there is a tendency toward the microcytic range. At nine months postpartum, the effect of pregnancy can be said to have disappeared. Comparison of the ante- and postpartum figures gives no evidence of any considerable disturbance of the hematopoietic system, but does demonstrate an even greater resistance of the blood picture to deviate from normal during pregnancy than during the remote postpartum period.

compounds are hydrolyzed by boiling for two hours after adjusting the pH to approximately 0.7. This is accomplished by adding 10 c.c. of concentrated hydrochloric acid to each 100 c.c. of urine.

The extraction depends on the size of the droplets of the solvent passing through the urine, the length of the urine column and the time of extraction. The apparatus illustrated by Fig. 1 has given satisfactory results in our hands. In order to avoid diluting the urine, the diameter of the tube containing the urine is varied according to the size of the sample as follows:

VOLUME OF SAMPLE IN C.C.	INSIDE DIAMETER OF EXTRACTION TUBE IN MM.	LENGTH OF EXTRACTION TUBE IN CM.
500	35	75
1,500	50	75
3,000	75	75
4,500	85	75

The distributor is made from sintered Pyrex glass as described by Kirk, Craig, and Rosenfels.¹⁰ Our extractions are carried out for a twenty-four-hour period, during which time approximately 80 liters of chloroform pass through the extraction column. Chloroform has been used in our work because of the fire hazard attached to benzene or ether. In our experience the use of a small gas flame has been very satisfactory.

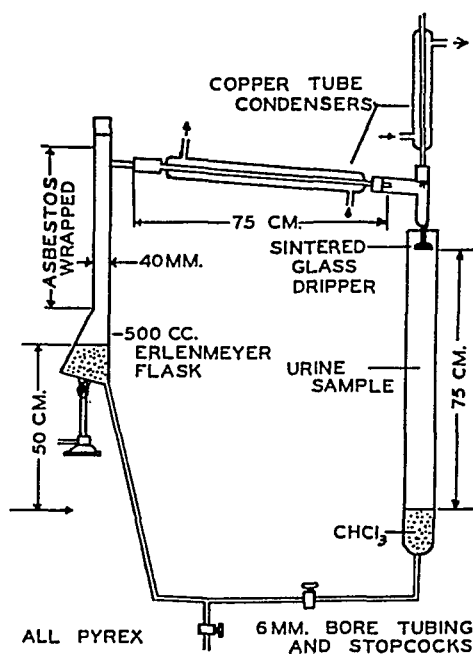


Fig. 1.

3. Partial purification without loss of active principles. Our procedure follows: The chloroform extract with the washings is evaporated to dryness on a steam bath. The chloroform is recovered. The residue is transferred to a 150 c.c. Erlenmeyer flask with alcohol. The alcoholic solution is evaporated to a volume of about 5 c.c. and transferred to a liter separatory funnel. The flask is washed with three portions of peroxide free ether, using a total of 100 c.c. of ether; then once with 10 c.c. of alcohol and finally with 25 c.c. of ether. The ether-alcohol solution is now shaken with 400 c.c. of 8.5 per cent sodium acid carbonate solution. The aqueous layer is separated and is then extracted three times with 100 c.c. por-

5. Study should be concentrated on those patients with hemoglobins of less than 60 per cent if our present knowledge of anemia in pregnancy is to be extended.

I wish to thank Mrs. K. Purviance, A.B., for her kind interest and technical assistance in the preparation of data presented in this paper.

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THE QUANTITATIVE DETERMINATION OF ESTROGENIC SUBSTANCES IN NORMAL FEMALE URINE DURING THE MENSTRUAL CYCLE*

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IN RECENT years a number of assays have been made of estrogenic substances in the urine of pregnant and nonpregnant women.¹⁻⁷ Allen and his coworkers have recently reported an analysis of the urine of the chimpanzee during the various stages of the menstrual cycle.⁸ These attempts to devise methods for an accurate quantitative assay of the estrogenic materials in normal female urine have been carried out in the hope that a basis might be obtained for the analysis of pathologic conditions such as sterility, amenorrhea, oligomenorrhea, menorrhagia, and also possibly uterine fibromyomas.

We now know that an accurate assay of the estrogens in urine depends on many factors, among which the following must have particular attention.

1. Faithfulness in collecting twenty-four-hour samples. This is especially difficult because of the inconvenience the average normal woman finds in saving all of the urine during the day. For this reason we have made some attempts to assay twelve-hour nocturnal samples.

2. Completeness of extraction. It is well established that the estrogens may occur in the form of conjugated compounds such as the glucuronate,⁹ which are insoluble in immiscible solvents, such as ether, benzene, and chloroform. These

*This investigation was aided, in part, by a grant from the National Research Council, Committee on Problems of Sex.

B. The dosage indicated was given in one injection in aqueous suspension. The readings were taken thirty-six hours later and then three more smears at eight-hour intervals.

C. The dosage indicated was given in olive oil in one injection and smears were taken as in "B".

D. The dosage indicated was given in olive oil in four injections at twelve-hour intervals and smears were taken as in "A".

Figs. 3 and 4 show some of our earlier assays of two succeeding menstrual cycles in which the *stock solution* from twenty-four-hour samples was evaporated to dryness and the residue suspended in 33 c.c. of olive oil. These urines were not hydrolyzed before the extractions were made. The material was injected into thirty rats. Each rat received 1 c.c. The urine was collected by a married woman (Mrs. R. G.), aged forty-four years, a bipara with normal menstrual history. It is interesting to note a peak in the excretion thirteen to fourteen days preceding the onset of the next menstrual period and a second peak within a few days of the next period. In order to make sure that the peaks were not vagaries of the extraction procedure, the total lipins were determined, and Fig. 3 shows no appreciable rise

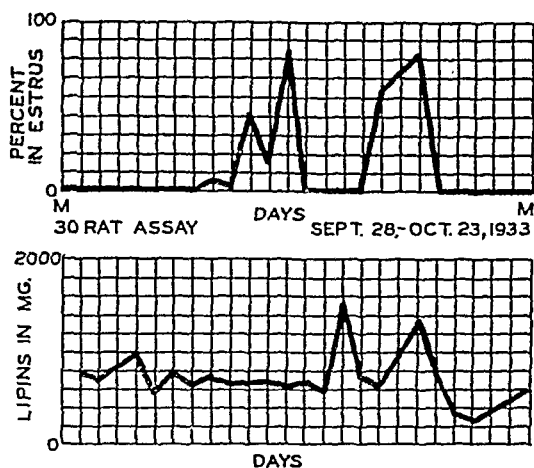


Fig. 3.

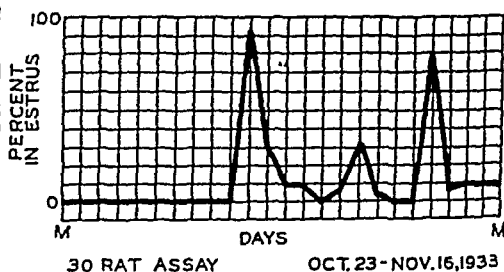


Fig. 4.

in the lipins at the peaks of estrogenic excretion. The estrin content at other times during the cycle was not sufficient to bring any animals into estrus when thirty animals were used for the assay. These graphs are typical of 17 that were obtained by this method.

Series K.: Mrs. A. B., aged forty-four, bipara, with regular and normal menses collected twenty-four hour samples. The urine of this series was not hydrolyzed. The residue from each day's extract was dissolved in 15 c.c. of 95 per cent alcohol.

Five cubic centimeters were reserved for a colorimetric assay which will be reported later. The remaining 10 c.c. were evaporated to dryness and emulsified with 60 c.c. of water and 0.2 gm. of di-glycol stearate. Ten rats were given four injections of 0.5 c.c. If all the rats showed positive smears, 22 c.c. of the solution were diluted with 11 c.c. of water and this was injected into 15 rats in the same way. Fig. 5 is the result of this assay. Again two peaks were found and this time the peaks were observed at twenty and fifteen days before the onset of menstruation.

Series K-2: Same subject as K. In this series it was hoped that an assay could be made of the twenty-four hour sample for the free and combined estrin. One-half of the sample was hydrolyzed by boiling with hydrochloric acid at pH of 0.7. The two portions were then extracted separately and the assay made as under

tions of ether. The ether extracts are combined and evaporated to dryness. The residue is then taken up in 15 c.c. of 95 per cent ethyl alcohol. This constitutes the *stock solution* for assay.

4. Method of assay. The most satisfactory assays that have been developed to date are modifications of the method of Allen and Doisy,^{11, 12} using the vaginal smear of the spayed rat. Workers differ slightly in what they regard as a positive reaction. We have used the full estrous smear; squamous epithelial cells and the practically complete absence of leucocytes. The work of Coward and Burn¹³ and Gustavson and D'Amour¹⁴ has shown that the accuracy of the assay depends on the number of animals used. This accuracy also depends on the method of administration of the materials for assay. This phase of the problem has been carefully studied by Marrian and Parkes¹⁵ and by D'Amour and Gustavson.^{16, 17} Two methods are in common use: (a) suspending the material in oil and injecting the material in one dose, and (b) suspending the material in water and dividing the dose between several injections. The latter method is the most sensitive and precise. We have used both methods.

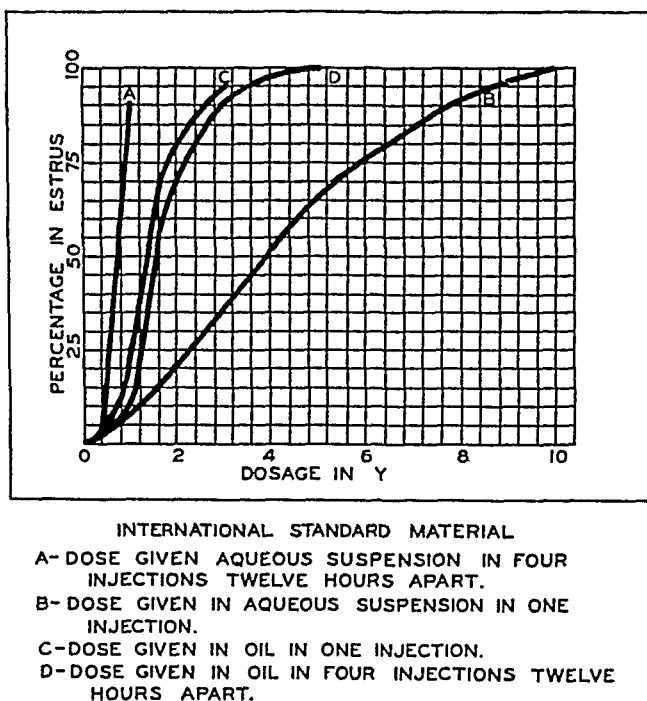


Fig. 2.

Our aim has been to report the estrogenic materials in International rat unit equivalents. The I.R.U.E. is defined as that amount of estrogenic material having the same biologic activity as 0.1 gamma of keto-hydroxy estrin, when the spayed rat is used for the assay. Fig. 2 shows the standardization curves for International standard estrin by four different methods of assay, using fifty spayed rats for each point on the curve. The curves were obtained as follows:

A. The dose indicated was injected in aqueous suspension in four portions at twelve-hour intervals. In making the suspension di-glycol stearate (0.2 gm. in 30 c.c.) was used. Smears were taken twelve hours after the last injections and three more smears were made at eight-hour intervals.

of estrogen in the hydrolyzed sample is increased but the relative excretion from day to day seems to be the same. All the results in this paper are calculated to a twenty-four-hour basis.

The most accurate method we have been able to devise after studying the problem for the past four years is as follows:

Six cubic centimeters of the 15 c.c. of *stock solution* are placed in a small mortar, 0.2 gm. of di-glycol stearate added and the mixture evaporated to dryness on the steam bath. Twenty-seven cubic centimeters of hot water are added in four portions and the mixture stirred thoroughly and the emulsion transferred to a large 20 mm. by 250 mm. test tube to which a stopcock has been sealed. These suspensions are then thoroughly shaken for fifteen minutes in a shaking machine. Very stable emulsions are formed. By drawing the emulsion into the syringe through the stopcock, foam is avoided. This material is injected into 10 rats, each rat receiving 2 c.c., divided into four doses of 0.5 c.c. The injections are made twelve

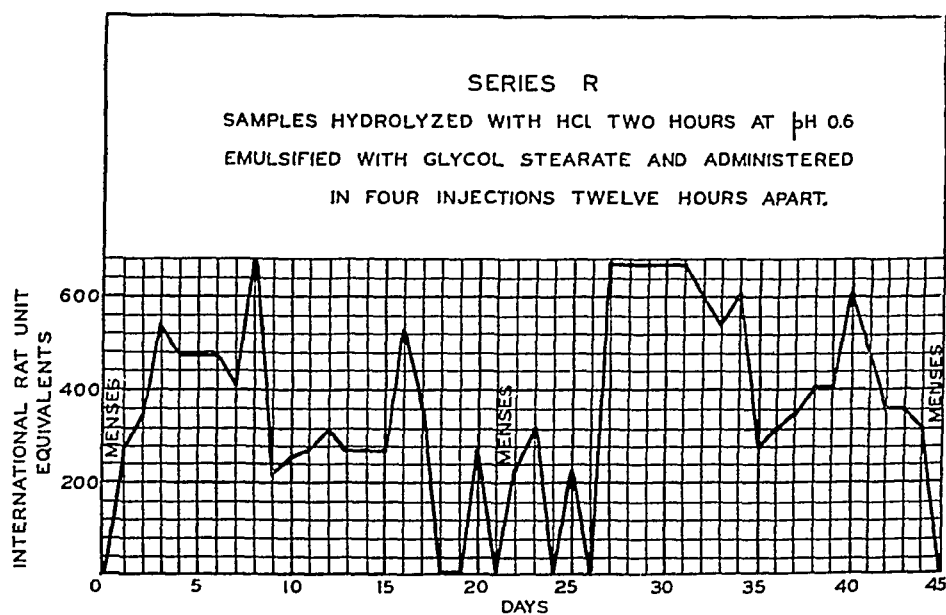


Fig. 7.

hours apart and the first readings taken twelve hours after the last injection. Three more readings are then taken at eight-hour intervals. The procedure from this point depends upon the response obtained. (a) If none of the animals respond, the remaining 9 c.c. of the *stock solution* are evaporated and suspended in 27 c.c. of water in the same manner as described, this dose being 1.5 times the original dose. This material is then injected into 10 rats. (b) If 4 to 8 rats give a positive response to the first injections, the remaining 9 c.c. of the *stock solution* are suspended in 40.5 c.c. and injected into 15 rats; this dose being the same as the original dose. (c) If all of the rats receiving the first injection respond positively, the remaining 9 c.c. of the *stock solution* are evaporated and suspended in 60 c.c. of water and injected into 20 rats in 4 doses of 0.5 c.c., this being one-half the original dose. Figs. 7 and 8 were obtained by this method.

Sample calculations of the amount of estrin in International rat unit equivalents are as follows: (a) 0.2 gm. of di-glycol stearate was added to 6 c.c. of the *stock solution*, containing the extract from a twelve-hour urine sample, and the solution evaporated to dryness. The residue was emulsified with 27 c.c. of water. This

K. The quantity of uncombined estrogens in the unhydrolyzed portion was so small that practically no response was obtained. Further attempts will be made to determine the free and combined estrogens in twenty-four-hour samples. From the study of the hydrolyzed portion Fig. 6 resulted. In this cycle the peaks of excretion

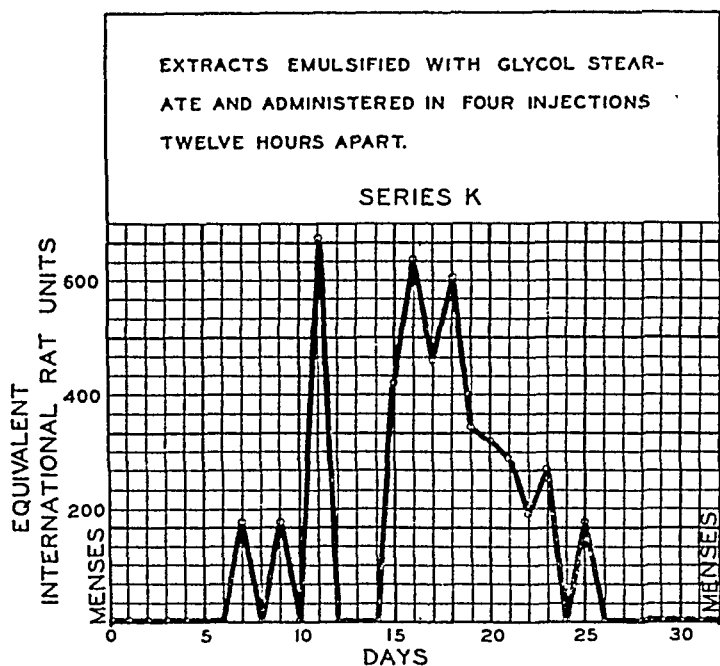


Fig. 5.

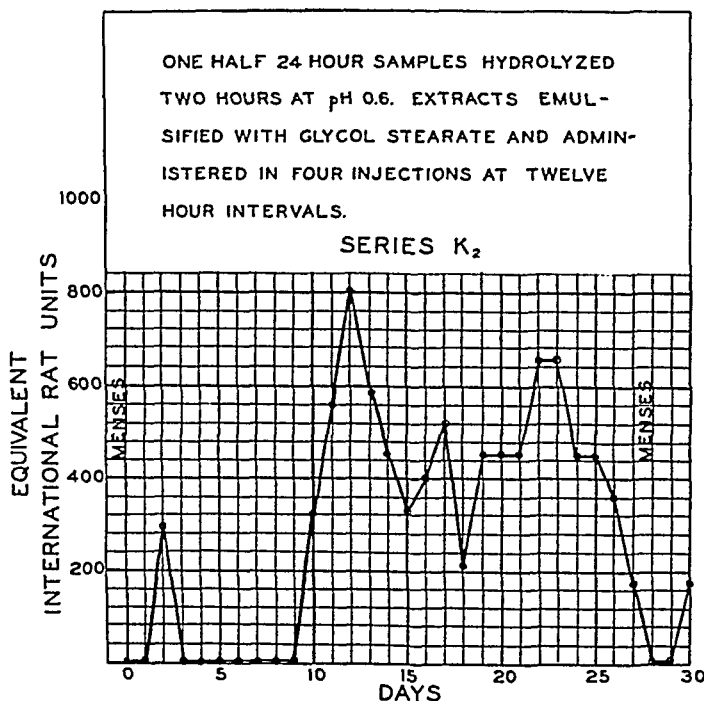


Fig. 6.

came sixteen and six days before the onset of menstruation. Fig. 5 showing the results of the assay of a twenty-four-hour nonhydrolyzed sample, and Fig. 6 showing the results of the assay of one-half of the twenty-four-hour hydrolyzed sample are very similar in form, from which it may be tentatively concluded that the amount

In the present state of our knowledge, the interpretation of these graphs, so far as they reflect, or are the result of, what is taking place in the endocrine system during the sex cycle, can only be speculative.

The thing which impresses one, as the graphs are viewed side by side, is that in each case, there are two peaks of estrin excretion, and by inference two peaks of estrin concentration in the blood. In some, this peak is sharp and reaches its maximum in one twenty-four-hour specimen. Less frequently a maximum is shown over a period of two days or more. After the first peak, there is a drop of varying degree, followed by another peak, and in every case the estrin excretion drops to zero at or very shortly preceding the next ensuing menstrual period.

In studying these graphs over a period of several years, we have come to think that the first peak is coincident with ovulation. We believe, however, that this point remains to be proved. It seems reasonable to believe that this peak represents the height of follicle activity, and that when it ruptures there is either a cessation or considerable diminution of its cellular activity. For a varying period of time following its rupture, before the growth of the lutein cells, one would expect a drop of estrin production. In the graphs, such a drop follows in every case the appearance of the first peak.

After the lapse of a certain amount of time, the structure is converted into the corpus luteum. We know that while this body is responsible for the formation of progesterone, it is also responsible for the continued formation of estrin^{18, 19} to as great, if not to a greater extent, than the follicle before rupture. If this is so, it could account for the second estrin peak which is present in all of the graphs. The regression of the corpus luteum, with a diminution or disappearance of estrin is followed shortly by menstruation. This coincides with our knowledge of the action of estrin when given to the human female after castration, viz., that bleeding follows the withdrawal of estrin, if the amounts administered were sufficient.

The graphs shown are those of three women, all entirely normal from gynecologic and general standpoints. Since a particular ovulation and developing corpus luteum are the controlling factors in the next subsequent menstruation, it is of interest to note what relation the peaks in the graphs bear to the time of the next menstrual period in each case. It can be seen that neither of the two peaks bears any constant relation to the time of the next menstruation, nor do they to each other. This variation is seen in the graphs of different individuals and in different cycles in the same individual.

It seems to us that these observations necessitate one of two conclusions: (1) either the time of ovulation may vary considerably from cycle to cycle in the same individual, and be considerably different in different individuals, and that the corpus luteum may require varying

material was injected into 10 rats, each rat receiving four injections of 0.5 c.c. Six of the animals came into estrus. In order to increase the accuracy of the assay, the remaining 9 c.c. were emulsified in the same manner with 40.5 c.c. of water. This gives the same concentration as in the exploratory assay. This suspension was injected into 15 rats in four injections of 0.5 c.c. Ten of the rats came into estrus, making a total of 16 out of 25, or 64 per cent. This corresponds to 0.82 gamma of International standard estrin per rat from Curve "A", Fig. 2. This is equal to 8.2 rat units. The number of International rat unit equivalents therefore, since 2 c.c. are equal to 8.2 International rat unit equivalents and the material

was placed in 67.5 c.c., is $\frac{67.5 \times 8.2}{2} = 276$, or if we assume the excretion for twenty-four hours to be twice that of twelve hours, the twenty-four-hour excretion is 552 International rat unit equivalents. (b) Six cubic centimeters of the *stock solution* of another extract of a twelve-hour sample were emulsified and injected into 10 rats as described in (a). None of the rats came into estrus. This makes

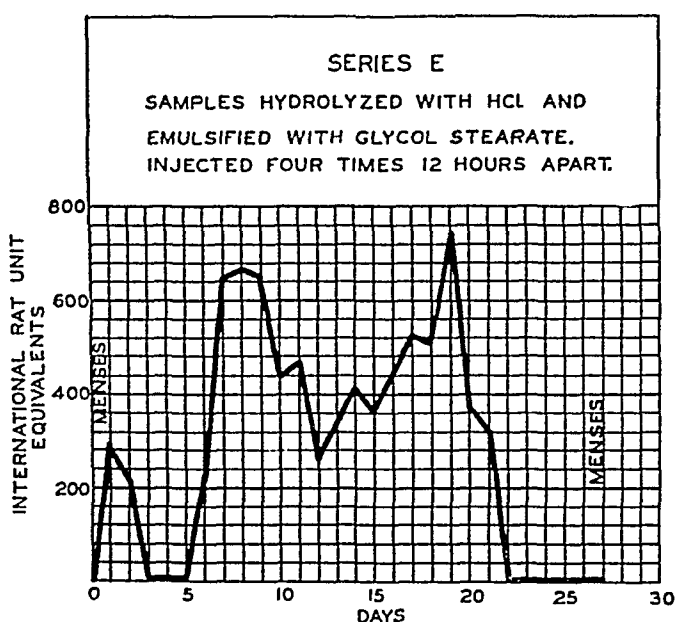


Fig. 8.

it necessary to use a higher concentration of the material. The remaining 9 c.c. of the *stock solution* were emulsified with di-glycol stearate in 27 c.c. of water and injected into 10 rats. Four rats out of the 10 came into estrus. Forty per cent corresponds to 0.65 gamma of International standard estrin per rat from the standardization curve, which equals 6.5 rat units. This amount was contained in each 2 c.c. of the 27 c.c., but this was only 9/15 of the total *stock solution*. The number of International rat unit equivalents is therefore $\frac{6.5 \times 27 \times 15}{2 \times 9} = 146$ or 292 for a twenty-four hour sample.

Fig. 7 shows the excretion curve obtained by this method of assay of urine, collected for twelve hours during the night from the same woman who contributed the urine for Figs. 3 and 4.

Fig. 8 shows the excretion from an unmarried girl (Miss R. E.), twenty-two years of age, using twelve-hour nocturnal samples. This girl had a normal menstrual history.

due almost wholly to insufficient preparation for extrauterine life and only slightly to obstetric trauma. We are particularly interested in discovering what may be done to lessen the loss of fetal life among the group of infants who have completed the term of intrauterine life and are prepared for independent existence.

TABLE I. INCIDENCE

Total deliveries	8,531
Breech	285
Babies	293
Incidence	3.34%

If a breech position is discovered as the pregnancy advances into the third trimester, what is the wisest course to pursue? Opinions have varied, one group advising that all breech positions be changed to cephalic, while another feels that they should be let alone, labor being permitted to begin with a breech presentation. Our position in this matter agrees with neither of the above. We rather definitely think, at about the end of the eighth month, that an attempt at external version should be made. This is done with the foot of the table elevated so that the breech may gravitate upward away from the inlet. Prior to labor the breech is rarely engaged. If, with the use of reasonable force the breech may be converted to a head position, we believe that the version should be carried out. We do not use anesthesia, believing that with the patient anesthetized, there is a tendency to use more force than is wise. If much force is needed, and after the exertion of moderate pressure upon the fetal poles the fetus fails to turn, the attempt is given up. There has been some difference of opinion as to the danger of the use of considerable force. We believe that there is sufficient danger to the child from drawing tight, loops of cord which may be about the neck or extremities, to warrant our rather conservative attitude. The delivery of a multipara of a child of moderate size in the breech position is often easy, and it does not seem wise to relieve the infant of a slight risk only to subject it to a greater one.

We much prefer that labor should begin spontaneously. Induction is only done when a rather clear-cut indication exists. We much prefer to have the membranes remain intact until dilatation is complete, or nearly so, although our experience has been that an early rupture is more frequent in breech cases because of the deficient filling of the lower uterine segment by the breech. The first stage in breech labor may be longer than in cephalic presentation and dilatation should be allowed to complete itself without interference. The use of some effective form of analgesia is often of great value.

periods of time to reach its full development and activity, or (2) the peaks of estrin excretion, presuming peaks of concentration in the blood, have no particular relationship to ovulation and corpus luteum activity. With the constancy with which these two peaks appear in the graphs used for these illustrations, as well as in all others obtained from daily twenty-four-hour specimens in normal individuals, the first conclusion seems to be more logical.

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A STUDY OF 285 CASES OF BREECH DELIVERY*

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THE fetal mortality attending breech delivery is far greater than that which accompanies deliveries in the cephalic position. We have studied the cases of breech presentation occurring in 8,531 cases in the department of obstetrics and gynecology in the Evanston Hospital. These numbered 285, an incidence of 3.34 per cent. This indicates a frequency slightly in excess of that usually quoted, which is 3 per cent. We have studied this series of cases to find out exactly what our results have been, and, if possible, to ascertain whether our results might not be improved. The fetal mortality in various reports and textbooks ranges from 7.6 per cent to 15 per cent at term. Many premature infants, not yet viable or so near the lower limit of viability that life expectancy is slight, are delivered as breech presentations. Little can be done to decrease the loss of life in this group as it is

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well than does the infant of normal size, and is also not as fully prepared for extrauterine life. In 187 cases, one infant weighing five pounds or more was delivered while in 20 others a twin weighing over five pounds was delivered by the breech. In these 207 deliveries there

TABLE II. FETAL DEATHS

Premature (under 7 mo.)	Deaths	27
	Macerated fetus	26 or 96%
	Monsters	1 death 1
	Twins	6 death 6
	36 delivered as breech	30—60 babies
	9 lost	25%
Term	188	Deaths 11—5.85%

were 18 deaths. Three of the infants which were lost were monsters. If these are excluded and the anatomically normal infants only considered, we find a mortality in this group of 7.3 per cent. In 40 cases in which the infants weighed less than five pounds there were 27 deaths. Three of these were monsters. Excluding the monsters and considering only the anatomically normal infants, we find a mortality of 64.8 per cent. The child which is near the end of gestation withstands the strain of delivery and that of independent existence far better than the premature infant.

TABLE III. INFANT MORTALITY—BREECH DELIVERY

WEIGHT	NO. CASES	MORTALITY	MONSTERS
<i>Single Deliveries</i>			
5 pounds and over	187	15	3
Under 5 pounds	24	18	2
Weight unknown	8	7	
<i>Twin Deliveries</i>			
5 pounds and over	20	0	0
Under 5 pounds	16	9	1
Weight unknown	-	-	-

A study was made of the influence of the infant's weight and the length of labor upon the neonatal mortality. The primiparas and multiparas are considered separately. Among the primiparas, of whom there were 94, with the exception of the group of very large infants, those weighing from 9 to 10 pounds, no great influence can be noted. While the group of very large infants is too small to be conclusive, there was one fetal death in five cases, a mortality of 20 per cent.

In the group of multiparas the lowest mortality appears in the group of large babies, those of 9 to 10 pounds in weight. In this group the lowest mortality is found in the subgroup of infants weighing 7 to 8 pounds. Among this number occurred a labor of twenty-seven hours, the longest recorded among the multiparas.

In cases of frank breech we greatly prefer to allow the breech to descend and for the hips to be delivered by the force of the uterine contraction, aided, if possible, by the voluntary efforts of the mother, before intervening. From that point on extraction by the method of Mauriceau is done. This is varied in some cases in that we may adopt the suggestion of Potter and deliver the anterior arm first. This we find in some cases to be an excellent maneuver, as the anterior arm is swept to the back as it is freed from the birth canal, thus bringing the shoulder and arm which was originally posterior to the front. The second arm is then often delivered with ease.

If this method is not easily applicable the older technic of freeing the posterior arm first is used. A common error is failure to continue extraction of the body of the infant until the tip of one scapula is visible. Attempts to deliver the arms before this time are likely to be far more difficult. We have found that two assistants to hold the legs of the mother is a much more satisfactory arrangement than the use of stirrups. These are objectionable upon three grounds: first, the thighs are so sharply bent upon the abdomen that it is difficult to follow down the fundus with the hand and more difficult to assist delivery by pressure upon the head above the symphysis. Second, the perineal structures are rendered more tense, and third, the pelvic inlet is slightly decreased in its anteroposterior diameter. If the thighs are held at an angle of about 130 degrees the operation is more conveniently done.

In cases of full double footling breech, especially if the feet come down into the vagina, intervention may be begun earlier.

In this series of 285 breech deliveries, the pregnancies varying in length from five months to term, there were 55 fetal deaths, or 18.8 per cent. Many premature infants are born in breech presentation. In this series there were 27 cases in which the fetus was of less than seven months' gestation.

The mortality in this group was 96 per cent. The chance of survival of infants of under seven months or of less than four pounds weight is so slight that we exclude them in estimating the mortality justly chargeable to obstetric technic. In the group of infants of over seven months' gestation were six monsters, none of which survived, and one macerated fetus which had died in utero before the onset of labor.

There were 188 cases of breech presentation in patients at or near term. In this group there were 11 fetal deaths, a neonatal mortality of 5.85 per cent.

A very marked difference is found if mortality of infants weighing five pounds or more is compared with that of infants under five pounds. The premature infant stands the trauma of operative delivery far less

exercised by the use of various anesthetics or analgesic drugs. The lowest mortality, 2.5 per cent, was found in the group of cases in which pentobarbital-sodium and scopolamine had been used as analgesics. Although we have used this combination extensively and have been pleased with our results, we do not maintain that these drugs protect the infant from the dangers of labor. We do believe that it is rather clearly shown that the administration of these analgesic agents does not increase the risk to which the infant is subjected. The maternal and neonatal results have been studied by one of us (C. E. G.) in two series of cases in which sodium-pentobarbital scopolamine was used. In a group of 96 women to whom no analgesic drugs were given, the mortality was 10.4 per cent, a greater neonatal loss of life than occurred with any form of analgesia or anesthesia. Those cases in which morphine or pantopon was used yielded the next highest infant mortality, 8.16 per cent. In order justly to assess the

TABLE VII. ALL BABIES WEIGHING OVER 6 POUNDS (185)

	CASES	MORTALITY	PER CENT
No drugs	96	10	10.4
Morphine	49	4	8.16
Pentobarbital	40	1	2.5
Drop ether	109	10	9.1
Gas	59	4	6.7
No anesthesia	14	1	7.1

influence of these drugs upon the infant mortality rate it would be necessary to study each history separately. Weighing all cases by the same standard it appears that the newer method of analgesia cannot be accused of increasing the neonatal death rate in breech cases. The death rate in cases in which drop ether was used, 9.1 per cent, seems high. It is probable that it is not wholly chargeable to the ether. This anesthetic is often used in cases in which some difficulty in delivery is anticipated.

Our cases were divided according to the type of delivery. In this tabulation all cases were included. Spontaneous delivery, in primiparas, including those delivered by manual aid, and breech extraction showed essentially the same mortality, 22 per cent and 23 per cent respectively. In this series, decomposition of the breech, followed by extraction, gave no mortality at all. In those cases in which the breech was decomposed a marked variance is found between the mortality in primiparas and in multiparas. Eighteen cases occurring in primiparas were so treated without the loss of a single infant. The same procedure, done upon 8 multiparas resulted in two fetal deaths, a mortality of 25 per cent.

Thirty-four women were delivered by cesarean section. It has been suggested that a breech presentation in a primipara constitutes an in-

An attempt has been made to estimate the loss of blood. Seven multiparas and 3 primiparas lost an amount estimated to be over 500 c.c. Sixty-three of 111 primiparas and 67 of 116 multiparas lost between 200 and 400 c.c. Packing of the uterus to control bleeding was done in the cases of 5 primiparas and 3 multiparas. The frequency of packing is probably greater than it would be in many other institutions, as we very definitely believe that packing should be done

TABLE IV. DURATION OF LABOR. MULTIPARAS

WEIGHTS	CASES	LONGEST	SHORTEST	AV. LABOR	FETAL MORT.
6- 7	27	16°	2° 15'	6° 8'	5
7- 8	24	27°	2° 30'	9° 12'	1
8- 9	18	17°	1° 37'	7° 8'	2
9-10	8	19° 45'	1° 16'	6° 23'	

TABLE V. DURATION OF LABOR. PRIMIPARAS

WEIGHTS	CASES	LONGEST	SHORTEST	AV. LABOR	FETAL MORT.
6- 7	38	34°	4° 30'	13° 33'	3
7- 8	25	55° 23'	2° 14'	14° 18'	1
8- 9	26	70°	2°	16° 21'	2
9-10	5	25°	6° 45'	17° 15'	1

early in the course of bleeding rather than late and that the preservation of the patient's own blood in her circulation is far better than the introduction of that of another individual after uncontrolled bleeding has created a serious anemia. A survey of the figures in Table VI does not indicate that a breech delivery is accompanied by a greater blood loss than a cephalic presentation. Loss of blood in breech deliveries is influenced, as in other cases, by exhaustion of the mother which causes the uterine muscle to act less efficiently, by relaxation of uterine musculature because of deep anesthesia, and by operative injuries. Attempts at delivery before dilatation is complete are especially likely to produce deep cervical injury which may cause bleeding.

TABLE VI. AMOUNT OF BLEEDING ALL CASES

	MULTIPARAS	PRIMIPARAS
Under 100 c.c.	15	15
100-199 c.c.	34	22
200-299 c.c.	29	45
300-399 c.c.	11	15
400-499 c.c.	5	8
Over 500 c.c.	7	3
Amt. not given	5	5
Uterus packed	5	3

All cases in which the infant weighed more than six pounds have been studied to ascertain what influence upon neonatal mortality is

4. in this series, only one child being lost. If dilatation is complete, and the child is alive, immediate delivery is indicated. Of the 30 cases in which labor was induced the bag was used only twice. Our use of the bag is sharply limited to some cases of placenta previa, an occasional case of premature detachment, and cases of toxemia in which a necessity for prompt response exists. Our results with the Watson method of induction, and lately with the rupture of the membranes in selected cases, have been so satisfactory that we have had little inclination to make use of metreuryesis.

TABLE X. COMPLICATIONS

		DEATHS
<i>Prolapsed cord</i>	4	1
<i>Induced</i>	30	4
<i>Third degree tear</i>	4	0
<i>Thrombophlebitis</i>	1	0
<i>Polyhydramnios</i>	3	3
<i>Postpartum hemorrhage</i>	10	2
<i>Uterus packed</i>	8	
<i>Toxemia</i>	6	4
<i>Broken humerus</i>	3	0
<i>Broken clavicle</i>	3	1
<i>Injured arm</i>	1	0
<i>Craniotomy; hydrocephalus</i>	1	0
<i>Ablatio</i>	1	1
<i>Fibroids</i>	2	1

The four third-degree tears which were recorded were repaired at once and in all four cases a satisfactory result was obtained.

In 11 cases there was postpartum bleeding. In 8 of these packing was used.

In difficult breech extractions it is sometimes difficult to avoid injury to the child. In 3 cases the humerus was fractured and in 3 others the clavicle. In one other case a slight Erb's palsy occurred which was followed by recovery. In cases in which it is difficult to bring down the arm a fracture of the humerus may occur. It is far better for the infant to suffer a fracture of the humerus than to have an injury of the musculo-spiral nerve or of the brachial plexus.

Injuries to the nerves of the upper extremity heal slowly and some loss of function may be permanent while injuries to the humerus heal rapidly. If a tiny wire splint is at once put on, an excellent result is usually attained. In our cases it has been impossible a few months later to tell which was the injured arm. We are indebted to our surgical colleagues for their help with these cases. The results in the cases of fracture of the clavicle were equally satisfactory. Prompt recognition is more important in bony injuries of the infant in order that necessary correction of possible deformity may be done at once. If any doubt as to the presence of bone injury exists, roentgenographic examination should be done.

dication for abdominal delivery. With this we do not agree. We believe that a reasonable indication exists when there is disproportion, caused either by a small pelvis or a large infant, so that the chance of delivering a living and uninjured baby through the birth canal seems less than normal. The great majority of our cases of breech presentation, including primiparas, were delivered without recourse

TABLE VIII. TYPE OF DELIVERY—MORTALITY

	MULTIPARAS			PRIMIPARAS		
	CASES	FETAL MORT.	PER CENT	CASES	FETAL MORT.	PER CENT
Spontaneous	28	7	25	9	2	22
Breech ext.	94	16	17	101	24	23
Breech broken up	8	2	25	18	0	0
Cesarean	6	1	16	29	3	10
Forceps on after-coming head	23	2	8	36	5	14

to section. The presence of any of the usual indications for cesarean section will justify the operation. With the tendency, too apparent in this country, to use cesarean section as a solution for all obstetric problems, its selection for the management of breech position should be carefully considered. A slightly greater latitude may be permitted in the cases of older primiparas but even here the mere fact of age does not outweigh all else. In our experience in all types of labor, our elderly primiparas have very little more trouble than our younger patients. Cesarean section should not be immediately decided upon merely because a primipara, whose infant lies in a breech position, happens to be a little older than the average. Table IX indicates the indications which caused the selection of abdominal delivery. Disproportion accounted for more than half the cases. Cesarean section occupies a definite place in the management of breech presentation, especially in primiparas, but should be reserved for those cases in which an adequate indication exists.

TABLE IX. CESAREAN SECTION

Disproportion	18
Toxemia	3
Recent fracture of pelvis	1
Placenta previa	2
Pulmonary tuberculosis	1
Repeat	3
Fibroids (Porro)	1
Heart	2
Indefinite	3
	<hr/> 34

A series of breech cases could scarcely be managed without some complications. These are indicated in Table X. Prolapsed cord occurs more easily in the presence of a breech presentation. There were

onset of parturition, but it is quite possible that in them the placenta may elaborate the same hormones as are produced by the ovaries of those in which the corpora are necessary to the end of pregnancy. In fact, there is some evidence that this may be so since in the castrated pregnant guinea pig the injection of estrin is not followed by an estrous response in the vaginal smear, the same inhibition being obtained as is obtained in the nonpregnant animal only when active corpora lutea are present (Courrier, Kehl and Raynaud, 1929). From this experiment it is assumed that the placenta elaborates an estrin-inhibiting substance. This may or may not be progesterin but highly purified progesterin-containing extracts of the corpus luteum are known to contain an estrin-inhibiting substance (Allen and Meyer, 1935). Recently numerous workers have reported the presence of progesterin in human placentas (Adler, de Fremery, and Tausk, 1934; McGinty, McCullough and Wolter, 1936; Ehrhardt and Fischer-Wasels, 1936; Mazer and Goldstein, 1932; Smith and Kennard, 1936). Consequently it is not illogical to suppose that the onset of parturition may be due in part to waning of the corpus luteum or to lowering of the progesterin level.

If parturition be due in part to waning of the corpus luteum, or to lowering of the amount of progesterin present, then appropriate corpus luteum extracts administered just before the onset of parturition should delay parturition.

The first successful experiments designed to test this supposition were carried out by Nelson, Pfiffner, and Haterius (1930). They found that the injection of a methyl alcohol extract of pigs' corpora lutea (doses equivalent to 10 gm. fresh tissue per day) into pregnant rats beginning on the fifteenth to seventeenth day of pregnancy caused a delay of parturition amounting to about two days in most instances. Miklos (1930) obtained essentially the same results also in rats using an alcohol-ether extract of the corpus luteum. At about the same time Allen and Corner (1930) found that pregnancy could be maintained to term by injection of progesterin in rabbits castrated the day after mating. Two of the animals reported by them actually failed to deliver at the usual time and delivery was accomplished by cesarean section on the thirty-fourth and thirty-sixth days. In both cases the fetuses were dead, but from their size it was apparent that some of them had survived to term, but in the presence of continued injection of progesterin, delivery had failed to occur. Mandelstamm and Tachikowsky (1932) found that a single injection of 1 c.c. of corpus luteum extract (cow) on the fifteenth to twentieth day of pregnancy in the mouse caused a delay of from four to ten days in 10 out of 12 animals. The manner of conducting the experiments was such that the exact amount of delay in each animal could not be stated, but the results are significant nevertheless. They also state that the period of delivery was prolonged and that the fetuses were of excessive size. Courrier and Kehl (1933) in a single case (rabbit) found that the injection of progesterin from the twenty-second to thirty-fifth day of pregnancy, the rabbit having been castrated on the twenty-second day, maintained the pregnancy and prevented the onset of labor and at the termination of injections autopsy showed all the fetuses to be fully developed but dead. More recently Portman (1934) has found that the administration of large doses of corpus luteum extracts (up to 6 Rb.U. per day) greatly prolonged the period of gestation in rabbits, in some in-

In one case craniotomy of the after-coming hydrocephalic head was done. This was preceded by tapping of the distended cranium by a trocar passed through the occipital bone close to the spine. No attempt should ever be made to deliver a hydrocephalic infant by the breech without lessening the bulk of the head. If, after this, delivery presents any difficulty craniotomy should follow.

CONCLUSIONS

1. External version should be done if possible by the use of moderate force.
2. Conservatism, operative intervention being withheld until an indication develops, is the wisest course.
3. The mortality rate is smallest in infants weighing five pounds or more.
4. The mortality of breech delivery at term in skilful hands should be less than 10 per cent.

636 CHURCH STREET

✓ PROLONGATION OF PREGNANCY IN THE RABBIT BY THE INJECTION OF PROGESTERONE*

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THE onset of parturition in many animals is preceded by regression of the corpus luteum and in some, such as the rat, mouse, and rabbit, removal of the corpora lutea is followed either by resorption or abortion of the embryos. In others such as the guinea pig (Herrick, 1928; Courrier, Kehl and Raynaud, 1929) and cat (Courrier and Gros, 1935), it is possible to remove both ovaries during the latter part of pregnancy without interfering with the progress of gestation in any way. The human being appears to belong to the latter group, since there are cases reported (Ask-Upmark, 1926) in which both ovaries were removed during the latter part without producing miscarriage. In the early part of pregnancy abortion usually follows removal of the corpus luteum (DeLee, 1916; Ochsner, 1920; Mackenzie, 1922). However, Pratt (1927) has reported two cases in which the corpus appears to have been removed at the very beginning of pregnancy (before a menstrual period had been missed) without abortion. In the human being and in those animals where castration can be performed without interrupting pregnancy, it would appear that the corpora could have no relation to the

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hour or so at most elapses between delivery of the first and the last fetus. It is also of note that in some animals delivery of dead fetuses occurred despite the continuation of injections. Rabbit 60 delivered two dead fetuses on the thirty-ninth day, one on the fortieth, and one on the forty-first day, injections being continued through the fortieth day. In cases where injections were stopped before delivery had taken place (18, 19, 20) delivery began within twenty-four to forty-eight hours. One animal in which postmaturity was very obvious by palpation (22) was delivered by cesarean section on the thirty-sixth day of 8 dead well-furred fetuses. The crown-rump length of these varied from 90 to 130 mm., indicating that they had survived for at least a day or two after the usual time of birth.

In practically all cases in which parturition occurred after the thirty-fourth day, postmaturity was apparent as judged by the size of the skeleton and amount of hair present, even though the fetuses at birth were not of excessive weight because of maceration.

Table 1
Prolongation of pregnancy with progesterone.

Table 1			Prolongation of pregnancy with progesterone.																		
Rabbit Number	Progesterone Daily	Injections started	Day of Pregnancy																		
			30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	
11	0.25	25	X																		
10	0.5	25	X																		
65	0.5	25				X															
9	1.0	25				X															
63	1.0	25					X														
64	1.0	25				X															
8	1.5	25												1		5 M					
20	1.5	25																4 M		3 M	
21	1.5	25						1 L 2 D 2 M 1 M													
18	1.5	20								9 M											
19	1.5	20									9 M										
22	1.5	28										8 M									
23	1.5	28						1 L 2 D 1 D													
59	2.0	25					9 L														
60	2.0	25											2 M 1 M 1 M								
62	2.0	25						9 L													

X, Spontaneous delivery of normal fetuses.

1 L, 2 D, 8 M, etc., one living, two dead, eight macerated, etc.

●, Young removed either by cesarean section or by autopsy. All others born spontaneously.

†, Exploratory laparotomy.

Solid black lines indicate period of injections.

1 mg. progesterone = 1 Corner-Allen unit = International unit.

The cause of death of the fetuses at about the thirty-fifth day was not always apparent. Rabbit 22, which was delivered by cesarean section of dead fetuses showing only very early maceration of the abdominal skin, had placentas some of which were still attached to the uterus. Another animal (20) was subjected to laparotomy on the forty-fifth day and one horn removed. The fetuses were large but badly macerated, the placentas all having been separated for a considerable length of time. The uterine wall in some areas appeared infarcted and section through such areas showed actual necrosis of the muscle presumably from pressure of the large, bony fetuses.

stances doubling it. However, the fetuses did not continue to grow indefinitely, since they were always macerated when autopsy was performed at the conclusion of the experiment.

Interference with parturition was accomplished in each case by these workers with extracts either known to contain progesterin or presumed to contain progesterin because of the method of preparation. It is more than probable that they also contained estrin since these researches were carried out before either estrin-free progesterin or progesterone were available. This fact makes it necessary to repeat the observations with progesterone before it can be said with surety that the inhibition of parturition obtained was due to the progesterin injected, especially since we (Allen and Heckel, 1936) have found that the injection of estrin during the latter part of pseudopregnancy in the rabbit causes the corpora lutea to persist in a functional state.*

EXPERIMENTAL

The following experiments were carried out to ascertain whether or not progesterone would cause inhibition of parturition in rabbits. The number of animals is necessarily small because of the small amount of pure progesterone available and the large amount required for each animal, but they seem adequate to establish that it does markedly interfere with the onset of parturition. Both natural and synthetic progesterone were used. The natural hormone was prepared from sows' ovaries by the method of Allen and Goetsch (1936). The α form alone and mixtures of α and β forms were used. The synthetic hormone used was of the α form and was donated by E. Merck, Darmstadt. One milligram of crystalline hormone is equivalent to one Corner-Allen rabbit unit and to one international unit.

Virgin does were mated and then injected with various amounts of progesterone, injections beginning on the twentieth, twenty-fifth, or twenty-eighth day of gestation and being continued either until parturition had occurred or until it had been significantly delayed beyond the usual time for delivery (i.e., thirty-two days). The results are set forth in Table I. In cases in which 1.0 mg. or less was given per day beginning on the twenty-fifth day normal parturition occurred at the usual time (9, 10, 11, 63, 64, 65). When 1.5 mg. or 2.0 mg. per day was given, parturition was significantly delayed in nine out of ten animals and in one for as long as forty-five days. The mechanism of parturition was also disturbed in that the duration was considerably prolonged. In some cases a normal fetus was delivered at about the usual time and then at some later time postmature fetuses were expelled. Rabbit 21, for example, delivered one normal fetus and two dead ones on the thirty-fourth day and three dead ones early on the thirty-fifth; Rabbit 23 delivered a living fetus of normal size on the thirty-third day and three dead postmature fetuses on the thirty-fifth day. This is in direct contrast to a normal delivery where only an

*Since this paper was presented for publication, experiments on the rabbit in which pregnancy was prolonged by injection of progesterone have been reported (Koff, A. K., and Davis, M. E.: *AM. J. OBST. & GYN.* 34: 26, 1937). By the injection of estrin in the rabbit, we have succeeded in prolonging the life of the corpus luteum of pregnancy as well as that of pseudopregnancy. Parturition is delayed when the corpora lutea are so maintained.

very thick, and beginning between the twenty-fifth and twenty-eighth day large amounts of milk can be expressed from the nipples, the glands being at this time indistinguishable from those obtained at the time of parturition on the thirty-second day. The actual production of milk is probably due to the secretion of a lactogenic hormone by the pituitary, but the hormonal factors precipitating the release of this hormone are not fully understood. In these experiments the injection of quantities of progesterone adequate to interfere with the onset of labor, appeared to have no effect on the secretion of milk. In two animals (18, 19) the injections were begun on the twentieth day, but this did not prevent the appearance of milk at the usual time. However, in animals in which the fetuses were retained for a long time (8, 20) the mammary glands receded markedly after about the thirty-fifth day, even though milk could be expressed from the nipples at all times after the twenty-fifth day. The reason for this has not been determined, but it may be due to the fact that the placentas become separated and nonfunctional shortly after the death of the postmature fetuses.

The amount of progesterone necessary to prevent or delay the onset of parturition appears to be large (1.5 mg. per day) when compared to the amount necessary to produce progestational proliferation in the recently castrated rabbit. It requires only 0.2 mg. (0.2 I.U.) per day for five days to accomplish this (Wintersteiner and Allen, 1934), but such a quantity is apparently not physiologic, because Allen and Corner (1930) found it to be inadequate to maintain pregnancy to term, about 1.0 unit per day (equal to 1 mg. of progesterone) for this purpose being necessary. Recently Makepeace, Corner, and Allen (1936) have found it requires 1 mg. per day for five days to desensitize the rabbit uterus to pituitrin (in vitro), and Allen and Heckel (1936) have shown that it requires 1.5 mg. per day after the fifth day to maintain pregnancy changes for an additional five days. These observations make it evident that in the rabbit large doses are necessary to bring about conditions in the uterus optimum for normal implantation. In view of this, it is not surprising that equally large doses are necessary to interfere with the onset of parturition. These doses are huge when compared to those being recommended for clinical use at the present time, but it must be openly admitted that the entire question of dose for human needs is unsettled. However, in clinical cases in which progesterone should theoretically give benefit but does not, it should not be condemned until a dose has been given which is more in accord with animal experimentation than those already in use.

CONCLUSIONS

The subcutaneous injection of 1.5 mg. (1.5 I.U.) or more of progesterone per day in rabbits, beginning as late as the twenty-eighth day of gestation, effectively delays parturition in most cases and may pre-

Observations were made on the mammary glands of all animals. In each case lactation began between the twenty-fifth and twenty-eighth day of pregnancy, as it normally does in rabbits of our colony, even though injections were begun as early as the twentieth day. At the thirty-second day the mammary glands were as well developed as those of untreated pregnant animals at term and copious amounts of milk could be expressed from the nipples. In those animals in which parturition was greatly delayed (8, 20, 60), the mammary glands slowly regressed even though milk could be readily expressed from the nipples.

Several animals were autopsied at the conclusion of the experiments and sections made of the ovaries to see if there was any effect on the corpora lutea but in none was there any evidence that their life had been prolonged. All were markedly degenerate microscopically and in gross they could hardly be recognized.

DISCUSSION

These experiments show that progesterone prepared either from pigs' ovaries or synthetically from stigmaterol delays the onset of parturition in most instances in rabbits if an adequate amount is given. The results for the most part are of the same type as those obtained by Snyder (1934) who introduced new lutein tissue into the ovaries of pregnant rabbits at about the twenty-fifth day by the intravenous injection of gonadotropic hormone. His thorough-going studies showed in a convincing manner that the presence of new lutein tissue at the time of expected parturition effectively prolonged the period of gestation to about forty days in most cases, although the fetuses appeared to live to only about the thirty-fifth day. The fact that our results with progesterone are similar to those of Snyder makes it apparent that the new corpora accomplished the delay obtained in his experiments by virtue of the progestin produced.

The results have considerable bearing on the rôle which progestin plays during pregnancy in the rabbit. Many experiments show that it is indispensable early in pregnancy, and in the light of these experiments, it is probable that it is required for nearly the entire span of gestation. Castration prior to the twentieth day results in resorption of the embryos and after the twentieth day in premature delivery (Hammond, p. 190; Courrier, Kehl and Raynaud, 1929). It is probable therefore that lowering of the progestin level in the body is responsible in part at least for the onset of labor, especially since raising the progestin level (as in the above experiments) prevents the onset of labor. The causes of the onset of labor in the human being may possibly be of similar nature even though the corpus luteum of pregnancy is not necessary throughout gestation because recent evidence makes it appear that the human placenta may produce considerable progestin.

The behavior of the mammary glands in these experiments is also interesting. It will be remembered that in the rabbit the alveolar system gradually grows during the first three weeks of pregnancy. Then during the next few days the alveolae begin to secrete, the glands become

therapy. Bizard and Jolivet,¹ however, were confident that arsphenamine therapy would have prevented the disastrous results which they obtained following the use of quinine iodo-bismuthate in two instances in which it was employed: in one, in which 20 injections were given to the mother, the child developed syphilides over the entire body and died two months after delivery, while in the other a miscarriage occurred after more than 10 treatments had been given. Galliot⁵ reported a group of 27 patients who received intramuscular injections of bismuth hydroxide, resulting in 85 per cent live births, while of 29 arsphenamine treated patients in the same clinic, 89 per cent live births occurred. Pouget¹¹ on the basis of 3 fetal mortalities during bismuth therapy, did not consider it as suitable in the treatment of syphilis complicating pregnancy. Zakon¹⁵ has reported a series of 21 pregnant women treated with bismuth salicylate, while 5 patients received bismuth and neoarsphenamine. Twenty-six full-term clinically healthy children, 25 of whom were serologically negative, were reported for the group. Six or more injections were given in all but 5 instances.

Notwithstanding the fact that bismuth therapy of syphilis in pregnancy has been limited, its use has been recommended by a number of eminent syphilologists, especially on the strength of its innocuousness, its high renal tolerance, its relative freedom from reaction and ease of administration. Schamberg and Wright¹³ conclude that: "bismuth may be successfully and safely given during the period of gestation and the period of lactation. Active lesions disappear rapidly, and in old cases, if treatment is begun early and continued throughout the period of gestation, the pregnancy comes to full term."

In the present report a study is made of 34 pregnant syphilitic women treated solely with bismuth, in the form of intramuscular injections of quinine iodobismuthate. The drug is a red precipitate suspended in oil, and, according to Levaditi,⁸ has a bismuth content of 23.85 per cent. Quinine iodobismuthate was introduced by Fournier and Gernot in 1921 and 1922. It received early recommendation by Cabouat² for the treatment of syphilis in pregnancy, for which it was also used by Bizard and Jolivet.¹

In a more recent report Oliver and Crawford⁹ give results indicating that quinine iodobismuthate is superior to bismuth salicylate in spite of its lower bismuth content. They suggest that the quinine and iodide may play a rôle as well as the ionic state of the bismuth.

MATERIAL AND METHODS

A total of 34 consecutively registered syphilitic pregnant women received antisyphilitic treatment with quinine iodobismuthate in the form of intramuscular injection of 2 c.c. of a 10 per cent suspension in oil. Each cubic centimeter of the drug contains approximately 30 mg. of metallic bismuth (N. N. R.).

All of the women who received treatment had positive Wassermann and Kahn reactions. Twenty-eight were colored and 5 were white patients. A history of antisyphilitic treatment in previous pregnancies was noted in only 4 women of this group; it was also observed, however,

vent it altogether. The fetuses become postmature, but do not live longer than the thirty-fifth day in utero. In many instances parturition itself is quite abnormal, the time required for delivery of the entire litter being several days.

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QUININE IODOBISMUTHATE IN THE TREATMENT OF SYPHILIS COMPLICATING PREGNANCY

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NUMEROUS studies have shown that syphilitic pregnant women if adequately treated, will be delivered of normal babies in a high percentage of instances. Arsenical therapy has thus far proved most efficacious in continuing the pregnancy to a successful termination. Bismuth as an adjuvant following the course of arsenical treatment has also been widely recommended. The treatment of syphilis in pregnancy with bismuth alone has received but scant attention. This method of therapy was strongly recommended by Cabouat² in 1923, only one year after the introduction of bismuth treatment for syphilis.

A review of the available literature discloses relatively few reports, chiefly from French clinics in which bismuth alone was employed in the treatment of syphilitic pregnant women. Cabouat² reported favorably on the treatment of four pregnancies with trepol (tartrobismuthate of Na and K), neotrepol, and quiniobismuth, in which four full-term living babies resulted, one of which was syphilitic. Le Louer and Galliot⁷ after treating 13 women, 10 by intravenous injection of colloidal bismuth, and 3 by intramuscular injection of the hydroxide of bismuth, conclude that the results compared well with those noted with arsenical

live births in more than 96 per cent of the pregnancies, while among the untreated mothers only 69.1 per cent had live babies (Chart 1).

An analysis of the six cases which resulted in stillbirths (Table II) indicates that syphilis was the only attributable cause of the fetal mortality in 5 instances, while in the sixth case in which there was a premature onset of labor in the seventh lunar month with a breech presentation followed by breech extraction, both syphilis and excessive birth pressure were given as possible causes of fetal death.

TABLE I. RESULTS OF TREATMENT WITH QUININE IODOBISMUTHATE

	ENTIRE GROUP	GROUP RECEIVING 6 OR MORE TREATMENTS	GROUP STARTING TREATMENT BEFORE SIXTH LUNAR MONTH
Pregnant women treated	34	20	12
Live births	28 or 82.4%	16 or 80%	9 or 75%
Stillbirths	6 or 17.6%	4 or 20%	3 or 25%
Miscarriages	None	None	None
Neonatal deaths	1 or 2.9%	None	1 or 8.3%
Babies living but clinically syphilitic	1 or 2.9%	None	None
Babies living and ap- parently healthy	26 or 76.5%	16 or 80%	8 or 66.7%

TABLE II. ANALYSIS OF FETAL AND NEONATAL MORTALITIES

OUTCOME OF PREGNANCY	ATTRIBUTABLE CAUSE OF DEATH	LUNAR MONTH TREATMENT STARTED	NO. OF TREATMENTS
Stillborn. Premature. Seventh lunar month.	Syphilis	4th	8
Stillborn. Premature. Seventh lunar month.	Syphilis. Excessive birth pressure?	5th	8
Stillborn. Full term. Macerated.	Syphilis	8th	4
Stillborn. Full term. Macerated.	Syphilis	9th	2
Stillborn. Full term. Dead before onset of active labor?	Syphilis	4th	17
Stillborn. Full term. Dead before onset of active labor?	Syphilis	6th	6
Neonatal death. Pre- mature. Seventh lunar month.	Syphilis? Prematurity?	5th	5

Of the 6 stillbirths, 2 were premature (seven lunar months), 2 were macerated when expelled at term, while in the other 2 indications of intrauterine fetal death were noted before the onset of active labor. It will also be noted that 4 of the 6 mothers who had stillbirths received 6 or more injections of quinine iodobismuthate.

The neonatal death recorded in Table II occurred in a child born prematurely at 7 lunar months, who was clinically syphilitic. The mother had received 5 treatments of quinine iodobismuthate starting in the fifth lunar month of gestation.

Reactions or toxic symptoms, immediate or remote, were not noted in any of the women treated with quinine iodobismuthate, nor were abortions or miscarriages induced. The injections with but few exceptions did not give rise to painful swellings. Abscesses did not occur in any instance.

that no fetal mortalities resulted from these pregnancies. Previous stillbirths or miscarriages were noted in 8 or one-third of the 24 multigravidas of this series.

Antisymphilitic treatment was given at weekly intervals from the time of registration until the termination of the pregnancy, except in those instances in which the patient did not return regularly for treatment. A total of 205 intramuscular injections of quinine iodobismuthate were given to 34 pregnant patients. Twenty women received six or more treatments. Only 12 patients, however, started treatment prior to the sixth lunar month of gestation. The largest number of injections given were 17, which were administered to two patients.

RESULTS OF TREATMENT

The outcome of the pregnancy among the 34 pregnant syphilitic women who were treated with quinine iodobismuthate alone is given in Table I. It will be seen

LIVE BIRTHS

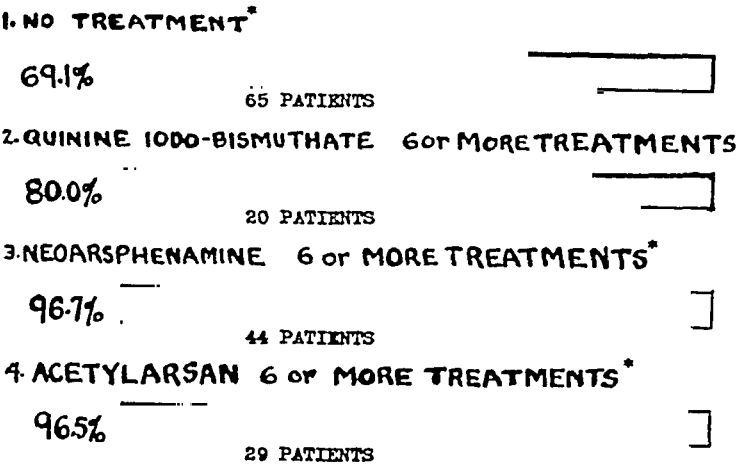


Chart 1.—Comparative efficacy of quinine iodobismuthate, neoarsphenamine, and acetylarsan.

that 6 (17.6 per cent) of the patients were delivered of stillborn babies. The remaining 28 women (82.4 per cent) had live births. Among the latter group one neonatal death occurred, while another child displayed evident signs of syphilis in the form of bullous skin lesions and “Snuffles” during the neonatal period.

Only 26 or 76.5 per cent of the total group were discharged with living apparently healthy children. Of the 12 cord blood Wassermann reactions taken among this group, 4 were positive, 6 were negative, and 2 were anticomplementary. It is the present consensus, however, that the result of the cord blood Wassermann reaction is of little significance; a positive result is an indication for further study of the baby, while a negative reaction does not eliminate the possibility of congenital syphilis.

Among a total of 20 women (Table I) who received 6 or more treatments with quinine iodobismuthate, 4 (20 per cent) had stillbirths; while among the 12 women who started treatment before the sixth lunar month, 3 (25 per cent) had stillbirths. In a previous study from this clinic, we³ demonstrated that six or more treatments during pregnancy with neoarsphenamine or with acetylarsan insured

The conflicting results of the clinical trial of bismuth preparations in pregnancy is evident from the review of the literature given below. The excellent results of treatment with bismuth salicylate, as reported by Zakon,¹⁵ are not in agreement with the results of the present study; in view of the clinical experience of Oliver and Crawford⁹ indicating that quinine iodobismuthate is superior to bismuth salicylate in the treatment of syphilis.

Since early and energetic treatment of syphilis in pregnancy may mean the difference between a living and a dead baby, intravenous arsenical therapy is to be desired in every case except where definitely contraindicated. In the usual dosage the arsenicals are tolerated as well, if not better, by the pregnant woman, than by the nongravid syphilitic patient.

When used in conjunction with the arsenicals, it cannot be denied that bismuth is of value in the treatment of syphilis in pregnancy. After a series of arsenical treatments it affords a safe and convenient method of continuing antisymphilitic treatment while the patient is given a rest before further arsenical administration. It deserves, especially, to be used simultaneously with arsenicals in syphilitic women who present themselves in the last weeks of pregnancy.

Abortifacient effects, due to bismuth, especially when combined with quinine, have been suggested as a contraindication by Bizard and Jolivet,¹ Juliusberg,⁶ and by Pouget.¹¹ This belief has not received general confirmation by other workers using bismuth alone, or bismuth as part of mixed treatment. In the present study not a single abortion or miscarriage occurred in spite of the observation that treatment was started with quinine iodobismuthate prior to the fourteenth week in 3 instances, and earlier than the twenty-eighth week in 23 instances. That no pregnancy was terminated earlier than the seventh lunar month may well be taken to indicate some protective influence exerted by treatment with this drug.

SUMMARY

1. A group of 34 pregnant syphilitic women were treated with quinine iodobismuthate by the intramuscular injection of 2 c.c. of a 10 per cent suspension in oil once a week.

2. Only 26 or 76.5 per cent of the total group were discharged with living apparently healthy children. Six babies were stillborn, one died neonatally, while another developed evident signs of syphilis.

3. Among 20 women who received 6 or more treatments, 4 (20 per cent) had stillbirths, while among 12 women in whom treatment was started before the sixth lunar month, 3 (25 per cent) had stillbirths.

DISCUSSION

Quinine iodobismuthate affords but little protection in successfully carrying a gestation to term as compared with women who received no treatment. In our hands it proved to be far inferior to neoarsphenamine and acetylarsan in similar groups of patients.

The results of Cabouat² and others indicate that treatment with bismuth, if started early in pregnancy, will offer adequate protection. This is frequently impossible in the ordinary clinic, where the majority of registrations occur in the last trimester. Further, it was noted that the results among patients who received more than 6 treatments with quinine iodobismuthate were no better than those obtained for the group as a whole. Early institution of treatment did not appear beneficial, a factor which is known to be of definite advantage in arsenical therapy.

It is probable that the failure of treatment in pregnancy by intramuscular injections of oil suspensions of bismuth alone can be attributed largely to its relatively slow absorption. In this respect the choice of quinine iodobismuthate was perhaps ill chosen for the present study in spite of its recommendation by early workers. As pointed out by Levaditi,⁸ "taking into account its feeble bismuth content in comparison with other bismuth preparations, quinospirol is to be recommended especially for courses of consolidation rather than for a treatment of attack."

The investigation of Sollman, Cole and Henderson¹⁴ indicates that bismuth preparations in oil suspension are absorbed less rapidly than those in oily solution, while the water soluble preparations are absorbed more rapidly than the latter. It has been demonstrated by Raiziss, Severac, and Moetsch¹² that the oil soluble compounds are only slightly more toxic than those in suspension, while those dissolved in water are considerably more toxic. It would seem that oil soluble preparations would be more suitable for the treatment of syphilis in pregnancy.

In addition to the question of absorption, the extent of placental transmission of bismuth is of practical importance in the protection of the fetus. The experimental work of Pack, Scharnagel, and Veal¹⁰ in pregnant rabbits and cats has demonstrated that with the usual therapeutic doses the amount of bismuth transmitted through the placenta is practically nil. Although bismuth was demonstrated in the fetal kidneys after the administration of toxic doses, it was found that pathologic changes were not induced until the amount of bismuth introduced into the pregnant animal approached 60 times the therapeutic dose for human subjects. More recently a small but irregular elimination of bismuth in the human uterine secretion during the course of therapy has been demonstrated by Durel and Manin.⁴

that other effects are produced by such treatment, it is safest to assume that beneficial results are derived from the heat created, and solely from the heat.

An understanding of the basic principles underlying the application of this form of therapy is important in considering the manner in which the effects are produced. The temperature rise is caused by the flow of short-wave current within the body. The wave in its passage, if it be an alternating or oscillating current, dissipates energy and produces heat. This can be explained by the manner of the electrical or molecular disturbance which takes place under the influence of the impressed voltage. As the current flows, the molecules are distorted, first in one direction and then the other; in effect, there is a vibration of these molecules, the vibratory rate being at the same frequency as the oscillating rate of the applied current and the intermolecular friction caused by this motion produces heat in the mass of tissues.

With ordinary diathermy current, the vibrations take place at the rate of only 600,000 to 1,000,000 per second, and because of this relatively low oscillatory rate, direct metallic skin contacts are required to introduce the energy into the body.

But when currents of extremely high frequencies are applied, such as those of short-wave length, the displacement of vibratory rate of the molecules will run from $12\frac{1}{2}$ to 30 million per second. Because of this very high frequency, we are able to introduce the current into the body without direct metallic contact.

In actual application of short-wave currents, there are two methods of introducing the energy into the body. One is commonly known as the condenser field method (pads) and the other as the magnetic field (inductance cable).

With the condenser field method, the metallic element in the insulated applicator pads is separated from the patient's skin by rubber or other insulation, and these metal plates together with the patient's skin form a condenser of small capacity. This small capacity would offer a tremendous impedance (or resistance) to the relatively long-wave lengths, such as are used in medical diathermy and such current would not flow. However, when the frequency is high enough (10 million or more oscillations per second) these capacities or condensers offer a negligible impedance, and the current flows freely from the metal plates through the insulating materials to the patient's skin, then through the intervening tissues, and out through the other condenser pads. Heat is created in the intervening tissue structures through the molecular activities engendered, as previously described.

If we remember that the human body consists of a multiplicity of cells of varying electrical characteristics, it may be reasonably considered to form many minute condensers, often with resistances in series

4. From a comparison with other groups of syphilitic pregnant women observed in this clinic it is concluded that quinine iodobismuthate afforded little protection to the pregnancy, and was markedly inferior to arsenical therapy.

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SHORT-WAVE THERAPY IN GYNECOLOGY AND OBSTETRICS

EXPERIENCES WITH ONE HUNDRED TWENTY CASES

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THE application and use of oscillatory electrical current of various frequencies in the different fields of medicine and surgery has been an extremely interesting excursion to watch. That it has been of value is attested by its steadily increasing application and various attempts to augment the scope of the differing physical procedures already in use. Within recent years waves of very high frequency, variously known as short wave, ultra-short wave, radiothermy, etc., have largely supplanted the interest in diathermy. It is rather obvious from the literature that some of the over-enthusiastic operators have confused therapeutic claims with indisputable results, but in spite of this rather human trait it is important that we evaluate this convenient and seeming practical method for producing deep-seated heat in any part of the body. Although claims have been made, notably by foreign writers, that the short-wave current produces physiologic effects other than heat, it has been difficult, in fact essentially impossible, to prove such statements. Therefore, while one may not forthwith dismiss the possibility

is found extremely convenient in treating irregular contours of the body such as a shoulder, neck, joints, etc., where physical structure makes application of the condenser pads difficult.

These two methods are described because one will be found more convenient for certain applications. It is doubtful if there is any therapeutic difference in the effects produced.

While I have spoken of the tendency to create greatest heat in the tissues of greatest conductivity, it is doubtful if practical differential heating can be accomplished and controlled due to the temperature equalizing effects in the tissues of heat conductivity and blood flow. In practice, one must assume that all body structures, lying between the plates of the condenser applicators or within the field of the inductance cable, must have temperature elevations of varying degree and duration.

Our interest in the possibilities of short-wave therapy in obstetrics and gynecology was aroused by its presumed ability to produce heat for conditions and in locations otherwise inaccessible to it in the usual form. In the several conditions herein reported it had long been felt that if heat could be applied adequately, safely, and easily, much benefit would be derived. It was decided to use short-wave therapy in such conditions as might conceivably benefit from tissue heat and the physiologic tissue changes resulting therefrom, and a course of therapy planned. All of the treatments were given on patients in the hospital and given under careful supervision and observation. Accurate records were kept, not only of the time intervals, the number of treatments, the obvious effect as determined from the clinical chart, and the eventual outcome, but also of the patient's response to this type of therapy so far as it concerned her subjective symptoms and most especially, pain relief. Many of the early treatments were given by one technician, although no highly trained operator is needed. The procedure was applied in different conditions encountered where application of heat might be expected to arouse local or general beneficial response. Nothing was expected over and above the ability of the modality to produce heat in the area treated.

RESULTS

Sixty-four patients who presented as the outstanding symptom infected and foul lochia, were observed and treated with short-wave therapy. Many of these were accompanied by tenderness of the uterus, and several were complicated by very high temperature and pelvic pain. Upon instituting short-wave therapy, it was noted that there was a marked increase in the lochia after the first or second treatment, subsequent to which there was a rapid or gradual change to normal. Where pelvic pain and uterine tenderness had been an outstanding symptom, the patient invariably reported symptomatic improvement. The foul lochia cleared in all but 4 of these 64, and in 2 cases the patient's condition progressed to general sepsis.

Seven of 8 cases of subinvolution of the uterus responded promptly to therapy, although 3 patients had been treated by the usual oxytocics without response. In

and in parallel. Thus, when dealing with a short-wave current, one may assume that once introduced into the body, the current will divide itself between resistive and capacitative paths and that the heat so created may be partly attributed to combinations of effects, viz., first a resistive heating in the resistive paths plus heating due to losses in many minute condensers.

We can visualize further freest passage of these currents through paths of low resistance, such as muscle, the vascular organs of the viscera, and the immediate subcutaneous tissues with their free peripheral circulation, and we can visualize that the current will tend to jump around or over the highly resistive tissues, such as bone, cartilage, fascia, etc., due to the condenser effect induced by these semi-insulators.

With the assumption that the freest current flow will take place in the good conductors (that is, the highly vascular moist tissues, the blood stream, etc.), whereas lesser current will flow in the semi-insulating tissues, we may presume that currents of very short-wave length (or very high frequency) will tend to seek out and flow freest through the most conductive structures. This may explain the apparent localization and beneficial effect on infected areas where edema or high aqueous content would create a low resistance, highly conductive path.

As previously stated, with the condenser field method, the current must flow from one applicator through all intervening structures and out through the second applicator. This is somewhat at variance with the second method of introducing short-wave currents into the body, viz., the so-called magnetic field or inductance cable applicator.

With the cable, heating is effected not by current passing through the body, but rather by the flow of secondary current induced in the body as the current flows in the coiled-up cable near or on the mass of tissue being treated.

Current from the generator is conducted through a flexible, heavily insulated cable which is either wound around the part to be treated or placed in the form of a flat "pancake" over the tissue where heat is desired.

Within the coiled cable, an alternating magnetic flux is set up by passage of the current. When a conductive body is placed in or near the coil, an electromagnetic force is induced which causes eddy currents of the same frequency as the current in the cable to flow in conductive parts of the body mass.

These eddy currents do not have to flow *through* intervening structures, but rather will they circulate within the various tissues. The greatest current will tend to flow and consequently greatest heat will be produced in the more conductive structures, without unduly heating the skin. Because of its flexibility and ease of application, the cable

one case there was a marked increase in bleeding amounting to hemorrhage, and this patient was subsequently found to have a large intrauterine piece of retained placenta.

In 10 cases of dysmenorrhea treated, the results were less startling. Mindful of the many possible causes of dysmenorrhea, it is not surprising that 4 failed completely of relief. None of these 4 showed gross pelvic abnormalities to account for the dysmenorrhea. In the 6 patients who had complete relief, the pain recurred in 4 at subsequent menstrual periods. However, in 3 of these 4 repetition of the treatment again effected temporary relief.

The most constant results were obtained in myalgias of the extremities, back, and neck, where the response was early and permanent and with a minimum number of treatments. These were in keeping with our knowledge of the response of myalgias of various forms to any type of heat therapy, wherein the amelioration of pain and tenderness depends largely upon heat effects of counterirritants, plasters, poultices, and similar forms of tissue heating applications.

The 12 cases of breast abscess recorded gave better results than the figures indicate. Seven of these came to incision and drainage, but the subsequent course could be fairly described as being less painful and associated with more rapid convalescence than one would ordinarily expect. Two cases ruptured before incision was made during the course of treatment, and in each instance there was a rapid subsidence in the infective reaction in the breast itself. In three instances inflammatory conditions in the breast, diagnosed clinically as breast abscess and showing marked tenderness, redness, induration of tissue, pitting edema of the overlying skin, and systemic reaction in the form of fever and headache, subsided after persisting treatment without incision and drainage and gave no subsequent trouble.

Ten patients with phlebitis were treated and clinical cure effected in 9 of these 10. The average period of disability was not much shorter than with other forms of therapy, but the relief to the patient came earlier and was more definite and lasting than those observed and treated by other methods. Analgesics were dispensed with in nearly all cases after the third treatment.

There was no increase in systemic temperature in any of the cases treated at the completion of any given treatment. Where any change in temperature was noted, it was in a downward direction.

COMMENT

The clinical impressions gleaned from this group of cases indicate that short-wave therapy is of real service in gynecology and obstetrics. An understanding of the patient and her condition, complemented by thorough appreciation of the physiologic changes induced by such treatment, is imperative before instituting therapy. The prompt and favorable response of the patient and the amelioration of pain in such diverse conditions as parametritis, myalgia, and phlebitis are too definite to be lightly dismissed. There were no untoward reactions nor complications due to the use of short-wave therapy in any of the cases observed, including those in which no benefit was obtained. The meteor length of the short wave used seemed to be of no clinical importance. There was no change in systemic temperature. Frequently, there was a marked improvement in the patient's general condition which was difficult to ascribe to the treatment; the intervention of psychic factors frequently plays a rôle in therapy of this form.

TABULATION OF CASES

DIAGNOSIS	NO. CASES	DAYS TREATED		AVERAGE NO. DAYS	NO. TREATMENTS		AVERAGE NO. TREAT.	NO. TREATMENTS BEFORE ANY IMPROVEMENT		AVERAGE NO. BEFORE ANY IMPROVEMENT	RESULTS
		MIN.	MAX.		MIN.	MAX.		MIN.	MAX.		
Foul lochia, endo- and myometritis Subinvolution of uterus	64	2	12	5.3	5	30	9.6	4	14	6.8	60 Satisfactory 4 No change 7 Favorable 1 Dilatation and curettage for retained secundines 6 Complete relief 4 None 14 Marked to complete relief 2 No relief 7 Incised and drained 2 Spontaneous drainage 3 Cleared without incision 9 Relieved completely 1 Improved
	8	1	4	2.1	2	12	4.7	2	4	2.8	
	10	1	1	1.0	1	2	1.4	1	2	1.4	
Dysmenorrhea	16	1	6	2.8	1	8	3.9	1	8	3.0	
Breast abscess	12	1	5	3.6	3	15	6.6	3	10	5.4	
Phlebitis	10	9	28	14.2	16	36	21.4	1	19	7.2	

POSTPARTUM HYPERTENSION FOLLOWING A NORMAL PREGNANCY

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(From the Obstetrical Out-patient Department of Touro Infirmary)

HYPERTENSION, observed at the routine examination six weeks postpartum, is not unusual, since it is frequently found in cases of nephritis, essential hypertension, or following certain toxemias of pregnancy. These increased pressures continue for a variable period of time, usually six to ten weeks, after which they return to normal, unless some degree of permanent kidney damage is present. On the other hand, postpartum hypertension after a perfectly normal pregnancy is an unusual condition and, up until the present time, it has been noted in the literature only once.

This condition was first called to our attention in 1934, when two patients presented themselves at the clinic in one afternoon. Several weeks later, I came across an article* dealing with the subject under discussion. After careful searching of the literature, no other reference was found. The purpose of this paper is to call attention to the existence of this finding, and to give the results of the investigation carried out, in an attempt to throw some light on its cause. The following statistics were obtained from the Out-patient Obstetrical Department of Touro Infirmary for the eleven month period from August 1, 1935 to July 1, 1936.

Incidence.—During the aforementioned period, 490 patients received the routine six weeks postpartum examination (279 white and 211 colored). Of this number, 23 cases, all colored, revealed postpartum hypertension after an apparently normal pregnancy. The incidence therefore is 1 in 21 or 4.6 per cent, as compared to Stout's reported incidence of 17.2 per cent. The latter's group, however, includes both white and colored patients, while as yet I have never seen a white woman display this phenomenon.

Age.—The age varied considerably, the youngest being seventeen years, the oldest, forty-two years, and the average, twenty-eight years. The group from twenty-one to thirty-one years comprised 56 per cent of the series.

Parity.—The series is composed of 4 primiparas (17.4 per cent) and 19 multiparas (82.6 per cent). Of the multiparas, there were:

Gravida 2—1
Gravida 3—4
Gravida 4—3

Gravida 5—2
Gravida 6—2
Gravida 7, 8, 9, 11, 12, 13, and 15—1 each

Stout's series consisted of 26.8 per cent primiparas and 73.2 per cent multiparas.

Period of Time Patients Were Observed During Prenatal Period.—When the patients in this series first enrolled in the prenatal clinic, 4 (17.3 per cent) were in the

*Stout, M. L.: Am. J. Obst. & Gynec. 27: 730, 1934.

The ease of application is notable. In all forms of pelvic pathology requiring treatment, the transabdominal application of pads was used. Many of the myalgias may be treated by the condenser field method using pads but in general are more conveniently managed with the inductive cable applicator. Both methods were used in this series. The reaction of the patient to this form of therapy is extremely interesting. Although at first a few were fearful, the majority were tremendously interested and almost invariably liked the treatment. The early pain relief undoubtedly accounted for the patients' favorable mental response.

The brief treatment time, which averages but fifteen minutes, the ease and safety of application offer advantages not to be found in other forms of heat therapy. No specially trained personnel is needed. There is scant danger of contact or spark burns with pads transmitting wave lengths under 20 meters, although accumulations of perspiration drops under condenser-field pads is guarded against by interposing an absorptive cloth.

The treatment time averaged fifteen minutes, the frequency one to three times a day. Treatments were continued until relief seemed permanent or until it was felt that persistence in heat therapy was useless. Beneficial effects were noted in from two to seven treatments. Excepting phlebitis, those conditions responding favorably required five days or less for satisfactory completion of therapy.

SUMMARY AND CONCLUSIONS

1. The theory and principles of short-wave therapy are considered.
2. The practical results in 120 cases are recorded.
3. Rigid adherence to valid indications and careful recording of experiences is urged, to properly evaluate the worth of the modality.
4. For the present, the beneficial results obtained are credited to the deep heat created only. It is not a "cure-all."
5. From our experiences, we believe short-wave therapy an exceedingly important method of treating certain gynecologic, postpartum, and postoperative conditions. We regard it as a valuable adjunct to present therapy.

39 GIFFORD AVENUE

Wood, J., Sabioncello, R., and Breiva, I.: Granulosa Cell Tumor of the Ovary. Bol. Soc. Chilena de obst. y ginec. (Buenos Aires) 2: 129, 1937.

The authors review the literature and report a case of granulosa cell tumor of the ovary. The treatment was operation followed by radiotherapy. Two and one-half years later the patient is in good health.

MARIO A. CASTALLO.

abnormal systolic pressure, the extremes being 134 and 200. Seven (30.4 per cent) were between 130 and 140; 15 (65.2 per cent) were between 140 and 180, and 1 (4.3 per cent) had a pressure of 200.

An abnormal diastolic pressure was found in 21 cases (91 per cent), ranging from 90 to 146. Eleven cases or 52.3 per cent were in the 90 to 100 group, 7 or 33.3 per cent in the group from 100 to 120, and 3 or 14.2 per cent ranging from 120 to 146.

It is interesting to note here that in three cases the pressure did not reach its maximum at six weeks. In Case 43589, the pressure at the postpartum examination was 136/92; four weeks later it had risen to 150/114, the rise being gradual and persistent. However, at the medical examination which was done forty-four weeks postpartum, the pressure was 118/80. Case 77739 showed a pressure of 162/80 six weeks postpartum; one week later it was 168/100, and the following week 154/110. Two weeks later (ten weeks postpartum) the pressure was 128/84 and it remained normal thereafter. She had received no treatment. Case 82348 had a blood pressure of 140/84 six weeks postpartum. One week later it was 142/90; the following week, 134/96. It returned to normal thirteen weeks postpartum.

Return of Blood Pressure to Normal: In most cases, a medical examination was not made until some time after delivery, so that a variable period of time intervened between the six weeks postpartum examination and that done in the medical clinic. For this reason, it is impossible to state exactly when the pressure returned to normal. Only in 8 cases was it definitely established that a normal pressure was finally attained during this study.

BLOOD PRESSURE AT 6 WEEKS EXAM.

2 cases reached normal 7 weeks postpartum	136/96; 144/90
1 case reached normal 9 weeks postpartum	144/96
1 case reached normal 10 weeks postpartum	162/80
1 case reached normal 12 weeks postpartum	136/96
1 case reached normal 13* weeks postpartum	140/84
1 case reached normal 14 weeks postpartum	134/96
1 case reached normal 44 weeks postpartum	136/92

*After thyroidectomy for toxic adenoma.

Of the remaining 15 cases, 3 did not report for medical examination. The other 12 still had hypertension when examined. An analysis reveals:

CASE	MEDICAL EXAMINATION MADE	BLOOD PRESSURE
144-805	6½ weeks postpartum	130/100
141-848	8 weeks postpartum	172/120
40067	9 weeks postpartum	172/118
139-142	12 weeks postpartum	188/124
62333	14 weeks postpartum	142/98
90419	15 weeks postpartum	192/112
25230	22 weeks postpartum	178/110
140-263	31 weeks postpartum	138/88
141-335	34 weeks postpartum	192/124
89344	36 weeks postpartum	142/100
22154	39 weeks postpartum	172/98
68518	40 weeks postpartum	170/110

Laboratory Data.—1. The Wassermann Reaction: All 23 cases had a Wassermann done; only in 2 patients was it positive, and then only weakly so, being one-plus. Some years previously, however, it had been three-plus. Of the remaining

first trimester of pregnancy, 14 (60.8 per cent) in the second, and 5 (21.7 per cent) in the third. The least number of prenatal visits a patient made was 3, and the greatest number, 16. The average number of visits made to the prenatal clinic was 9. Nineteen patients (82.6 per cent) made 6 to 16 visits.

Blood Pressure During Pregnancy.—On our service at Touro Infirmary, we consider a systolic pressure of 130 and over and a diastolic of 90 and over, as abnormal. Sixteen patients of the series neither during pregnancy nor labor exhibited an abnormal pressure at any time. The remaining 7 cases did go slightly above the normal mark occasionally, but due to the marked increase postpartum, these cases are added. An analysis of this latter group reveals:

CASE 136-967.—Enrolled when twelve weeks pregnant. Blood pressure 130/70; at second visit two weeks later it was 134/80; for the following nine to ten weeks her pressure ranged from $\frac{112-120}{70-80}$; when twenty-five weeks pregnant, her pressure was 140/80, after which it returned to normal with no treatment, and remained so, even through labor. At the postpartum examination, her pressure was 134/96.

CASE 25230.—Enrolled when about sixteen weeks pregnant. Blood pressure was entirely normal until patient was thirty-six weeks pregnant, at which time it rose to 120/94. One week later it was 134/94, the following week, 120/94, and the next week 112/80. Thirteen days later, she went into labor, the blood pressure rising to 148/90. At the postpartum examination, it was 160/146. This patient gave a history of having had hypertension four years previously, following a miscarriage.

CASE 139-142.—When this patient was twelve weeks pregnant, an electrocardiographic reading was done, and evidence of myocardial damage found. Diagnosis: Congenital heart disease (patent ductus arteriosus). The blood pressure at this time was 118/64. Maximum blood pressure during pregnancy was 134/84. (No other information available.) During labor, 140/80. Six weeks postpartum it was 176/110.

CASE 90419.—Enrolled when twenty-four weeks pregnant. Blood pressure normal until four weeks later, when it rose to 132/85. It remained abnormal for six weeks, the maximum reading being 136/88. For the remaining six weeks, the pressure varied from a low of 108/70 to a high of 128/84. No blood pressure reading was made during labor. At the postpartum examination the pressure was 180/110.

CASE 140-263.—Enrolled when thirty-five weeks pregnant. Blood pressure at this time was 114/60. The following week it was 130/80. She was given a salt-free diet and the succeeding two weekly readings showed the pressure to be 116/70 and 110/60. The pressure was not recorded during labor. At the postpartum examination it was 174/100.

CASE 90076.—Patient enrolled when twenty-six weeks pregnant. Pressure $\frac{110-120}{60-70}$ until six weeks later, when it rose to 140/82. The next three visits revealed pressures of 148/88, 138/66, and 120/90. The only form of treatment was a salt-poor diet. For the last four weeks of pregnancy, it rose to 160/94. At the postpartum examination it was 156/104.

CASE 106-619.—Patient enrolled when twenty-five weeks pregnant. Blood pressure ranged from $\frac{120-128}{78-88}$ until two days prior to onset of labor, when it rose to 128/90. The following day it was 134/90. No pressure reading was taken during labor. Six weeks postpartum, it was 170/110.

Postpartum Examination.—*Hypertension.* It was amazing to note the marked increase in pressure in some of the cases. All 23 patients in the series showed an

Patients in This Series Who Are Pregnant at the Present Time.

CASE 90076.—Blood pressure was 156/104 at the six weeks postpartum examination. She did not return for medical examination and how long the hypertension persisted is not known. She is at the present time twenty-five weeks pregnant and her pressure has ranged from $\frac{98-118}{44-76}$.

CASE 68518.—Blood pressure ranged during last pregnancy from $\frac{110-126}{74-88}$. Six weeks postpartum it was 178/140. At the medical examination done when forty weeks postpartum it was 170/110. At present she is about thirty-two weeks pregnant and her pressure has been persistently high, ranging from $\frac{130-144}{80-90}$. This patient is in her seventh pregnancy and apparently is a chronic nephritic.

CASE 77739.—Blood pressure normal during pregnancy. At six weeks postpartum examination it was 162/80. Two weeks later, diastolic pressure rose to 110. Pressure returned to normal thirteen weeks postpartum. At the present time this patient is about twenty-seven weeks pregnant. Her pressure has ranged from $\frac{96-110}{50-70}$.

SUMMARY

1. Twenty-three cases, all colored patients, of postpartum hypertension following apparently normal pregnancy are described.

2. The incidence was found to be 4.6 per cent of all the postpartum cases examined, both white and colored.

3. Fifty-six per cent of the series were between twenty-one and thirty-one years of age.

4. 82.6 per cent of the patients were multiparas.

5. The average number of prenatal visits made was 9.

6. Sixteen patients in the series had blood pressure readings lower than 130/90 during pregnancy. The remaining 7 cases are added due to the marked rise postpartum. An analysis of this latter group is given.

7. All patients revealed increases in pressure at the routine six weeks postpartum examination.

8. Only in 8 patients in the series was it definitely established that a normal blood pressure was eventually reached.

9. The results of the laboratory work are shown.

10. Postpartum medical consultation showed definite organic disease in 9 cases.

11. Three patients in this study have become pregnant again, and an analysis up until the present time is given.

CONCLUSIONS

Hypertension, following normal pregnancy, is a relatively unstudied problem, since it has appeared in the literature only once previously.

21 patients, 3 had received anti-syphilitic treatment during the recent pregnancy because of a previous positive reaction, or because of a history of having taken anti-syphilitic treatment at some other time. The latter is routine in our clinic to avoid any possible latent infection from escaping treatment during pregnancy.

2. *Fischberg Concentration Test*: This test was done on 16 of the patients. In 10 cases, it was low, the urine concentration never reaching the normal, 1.024. The remaining 6 cases revealed perfectly normal findings.

3. *Phenolsulphonephthalein Excretion*: Nineteen patients reported for this test. In 7 cases, it was 50 per cent or below for two hours. Three of this particular group also had a slightly subnormal Fischberg; 2 had normal Fischberg, and the remaining 2 patients had no concentration test done. On the other hand, in 6 cases of low urine concentration, the phenolsulphonephthalein excretion was normal.

4. *Intake and Output*: Of the tests done in 10 patients, 8 were normal. The other two, however, were far below par, the output being 18 per cent and 30 per cent of the intake (Cases 89344 and 62333). In both of these cases, the concentration test was normal, while the phenolsulphonephthalein excretion in the first case was 45 per cent, and normal in the latter case.

5. *Blood Chemistry*: This was performed on 18 patients, 15 of which were normal. The other 3 (Cases 102-504, 68518, and 25230) showed abnormally high uric acid content, being 6.12, 5.68, and 5.33, respectively.

6. *Blood Picture*: Blood counts were done on 18 patients; of this number, 6 had red cell counts of less than 4,000,000. Six also had a hemoglobin content of less than 70 per cent. None of the latter were in the former group.

Medical Examination.—Only 19 patients of the group presented themselves at the medical clinic for examination. Nine cases revealed sufficient evidence upon physical examination for a diagnosis to be made. These are:

Case 23632 Mild hyperthyroidism

Case 25230 Arteriosclerosis; possible chronic nephritis

Case 139-142 Congenital heart disease

Case 141-335 Arteriosclerotic heart disease

Case 77739 Hyperthyroidism

Case 82348 Syphilis; toxic adenoma

Case 22154 Heart disease; arteriosclerotic vs syphilitic; chronic nephritis

Case 62333 Toxic adenoma

Case 40067 Hypertensive heart disease

The following patients had no medical examination and the diagnoses given are merely made from the data available:

Case 136-967 Syphilis

Case 90076 Syphilis

Case 106-619 Syphilis; possible chronic nephritis

Case 47078 No diagnosis made

The remaining 10 cases had a physical examination but no evidence of any pathology, so that diagnosis was only possible from the laboratory data. These were:

Case 91300

Case 102-504

Case 43589

Case 68518

Case 142-464

Case 140-263

Case 89344

Case 144-805

} Possible chronic nephritis

No diagnosis could be made in Cases 141-848 and 90419.

to the growing products of conception and possibly a slightly increased activity of the thyroid gland. DeLee's only comment is that there is an increased basal metabolic rate during normal pregnancy, without hyperthyroidism. Hughes reports the largest number of basal metabolic readings, a total of 1250. His figures show a small increase at the sixth week of pregnancy, followed by lowered readings in the second, third, and fourth months; then, a gradual rise to a plus quantity, with a majority of the readings within normal limits, and in the last trimester an increase of plus 15 to 25 per cent. (This article seems to be the most complete in the literature from the clinical aspect.)

Supporting the theory of increased protoplasmic tissue as the cause for higher basal metabolic readings, Cornell and Baer report an abnormal rise in the basal metabolic rate during pregnancy, with a wide and nonconstant variation. They believe the death of the fetus in late pregnancy can be detected by a lowering in the maternal basal metabolic rate compared with the average of their series. This result they attribute to the cessation of the growth demands of the fetus and placenta. Sandiford and Wheeler found no evidence to suggest any change in the actual rate of intensity of heat production per unit mass of maternal tissue. Pommerenke, Haney, and Meek, by experimental work computing body surface areas of mother and baby rabbits and total heat production before and after delivery, conclude there is no actual increase in maternal basal metabolism.

Marine believes simple hypertrophy with some increased activity of the thyroid gland, amounting to more than enlargement incident to an increased blood supply, is present in women during puberty, menstruation, and pregnancy. Reyecraft reports that up to 50 per cent of women in Ohio show enlargement of the thyroid during pregnancy, with a considerable increase in the basal metabolic rate. Seitz claims 70 to 80 per cent of patients show hypertrophic changes in the thyroid gland, due chiefly to increased vascularization and epithelial elements with a storage of colloid toward the end of pregnancy, and disappearing three or five days before the onset of labor. Bockelman and Scheringer report laboratory findings on the iodine content of the maternal blood: 15.5 gamma per cent at the second month, 22.5 gamma per cent at the tenth month, and a definite decrease during the first two weeks postpartum. Stewart and Menne concluded from experimental work on pregnant rabbits that there is limited but definite evidence that iodine lowers basal metabolic shock incident to pregnancy. This conclusion is based on lowered basal readings and less active thyroid glands recorded for animals receiving iodine daily.

Actual increases in basal metabolic readings during pregnancy recorded in the literature range from plus 4 per cent to plus 35 per cent above normal just prior to the onset of labor. Practically all authors agree that there is a gradual return to the normal level during the first ten to fourteen days postpartum.

Many difficulties are encountered in the making of basal metabolic rates, and, despite all carefulness and precaution, various extrinsic factors may affect this examination of the patient.

The technic used in obtaining the basal metabolic rates in this series of cases is as follows:

1. Patient was at rest in bed for twelve to fourteen hours previous to the beginning of the test.
2. Patient given nothing by mouth except water, and not that for two hours previous to the beginning of the test.

Apparently it is predominately a disease of the colored race, although Stout has found the same condition in white women. The cause is unknown, but a few possibilities are suggested:

1. The result of the strain of labor. (This is improbable, since colored women usually have the easiest labors.)
2. The added stress put upon the kidneys in eliminating substances no longer necessary after pregnancy.
3. Since about one-third of the cases returned to normal seven to fourteen weeks postpartum, the cause might lie in an endocrine imbalance, in the attempt to become regulated to the normal, nonpregnant state.

I wish to express my appreciation for help and cooperation in examining these patients, to Dr. Charles Jones, of the medical clinic.

301 MEDICAL ARTS BUILDING

THE BASAL METABOLIC RATE IN NORMAL PREGNANCY*

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THE basal metabolic rate during normal pregnancy is not thoroughly understood. While there are numerous articles in the literature concerning this subject, the various authors lack a unanimity of opinion as to the interpretation of their findings. It is generally conceded that the basal metabolic rate is increased during normal pregnancy, and is due to either of two factors, or a combination of them. These factors are: (1) The increased protoplasmic mass of pregnancy; and (2) simple hypertrophy and hyperplasia of the thyroid gland.

Moderate hypertrophy of the thyroid gland has been more or less generally accepted as incident to pregnancy, to meet physiologic needs. Slightly less than 50 per cent of pregnant women are said to have some enlargement of this gland. The majority of authors do not attempt to give any definite conclusions as to the cause for the varying increases in the basal metabolic rate that all of them report.

Root and Root state there is a marked increase in the basal metabolism during the latter months of pregnancy, both in the total number of twenty-four-hour calories and in the number of calories per unit of weight. Plass and Yoakam believe a rise in the basal metabolic rate greater than plus 15 per cent, with a slower return to normal, suggests increased thyroid activity incident to pregnancy. Murlin, and others show an increase in the basal metabolic rate of plus 4 per cent. Many authors believe this rise so small as to be easily within the realm of normal error and variation. Williams writes that the increase in basal metabolic rate can be attributed

*Presented before the Obstetrical Society of Philadelphia, May 6, 1937.

III. CASES WITH ONLY TWO BASAL METABOLIC RATES DONE

(No omissions)

	PREGNANCY		POSTPARTUM
	1.	2.	
Number of patients in group	22	0	22
Average number of days of pregnancy or puerperium	155	0	9
Average weight of patients (pounds)	125.47	0	122.9
Average basal metabolic rate	8.1	0	3.1

(Omitting 9 cases because they do not follow the general trend of the readings)

	1.	2.	3.
Number of patients in group	13	0	13
Average number of days of pregnancy or puerperium	147	0	9
Average weight of patients (pounds)	129.44	0	126.56
Average basal metabolic rate	14.1	0	0.6

IV. CASES WITH ONLY ONE BASAL METABOLIC RATE DONE ON PATIENT

	PREGNANCY		POSTPARTUM
	1.	2.	
Number of patients in group	5	0	0
Average number of days of pregnancy or puerperium	127	0	0
Average weight of patients (pounds)	122.65	0	0
Average basal metabolic rate	11	0	0

There were no patients included in these groups who showed any signs clinically of any thyroid disturbance, although approximately 40 per cent showed slight enlargement of the gland to palpation. Eleven patients showed various signs of mild toxemia of pregnancy. The average basal metabolic rate for them:

Group I	18	19	16	(5 cases)
Group II	11		3	(6 cases)

There were no cases of severe toxemia. One case of eclampsia developed in a patient who did not attend clinic regularly. She was delivered in another hospital by cesarean section, and no postpartum basal metabolic rate was done.

SPONTANEOUS CASES

	Group I				Group II		
Morbid (4 cases)	15	13.6	8.7	(5 cases)	7.4	11.0	
Nonmorbid (16 cases)	7	13.0	2.2	(16 cases)	9.9	0.6	

OPERATIVE CASES

	Group I				Group II		
Morbid (2 cases)	3.5	11.0	0.5	No cases			
Nonmorbid (8 cases)	9.4	19.2	10.6	(1 case)	-16	3	

There were 30 patients who had the complete study of three basal metabolic rate tests; two prepartum, at approximately the fifth and the ninth lunar months, and one postpartum on the day before discharge from the hospital, usually the ninth day.

3. Majority of the tests made by the same two individuals.
4. Sanborn portable motographic machine used. The examination is based on the amount of oxygen consumed by the patient in a period of any consecutive eight minutes.
5. Examinations were made approximately at the fifth and the ninth lunar months and on the ninth day postpartum.
6. Patients examined, only those women having an apparently normal and healthy prenatal course.

The following results were obtained (figures indicate rate above zero):

I. TOTAL CASES

(No omissions for any cause)

	PREGNANCY		POSTPARTUM
	1.	2.	3.
Number of basal metabolic rates in group	57	30	52
Average number of days of pregnancy or puerperium	133	245	9
Average weight of patients (pounds)	124.44	141.53	123.64
Average basal metabolic rate	8.2	14.6	4.1

(Omitting 5 cases from group as only first basal metabolic rate was done)

	1.	2.	3.
Number of basal metabolic rates in group	52	30	52
Average number of days of pregnancy or puerperium	143	245	9
Average weight of patients (pounds)	124.44	141.53	123.64
Average basal metabolic rate	8.3	14.6	4.1

(Omitting 9 cases because the rates do not follow the general trend of the readings)

	1.	2.	3.
Number of basal metabolic rates in group	34	21	34
Average number of days of pregnancy or puerperium	144	245	9
Average weight of patients (pounds)	127.24	144.07	126.27
Average basal metabolic rate	9.7	15.6	2.4

II. CASES WITH ALL THREE BASAL METABOLIC RATES DONE ON PATIENT

(No omissions)

	PREGNANCY		POSTPARTUM
	1.	2.	3.
Number of patients in group	30	30	30
Average number of days of pregnancy or puerperium	133	245	9
Average weight of patients (pounds)	123.98	141.53	124.18
Average basal metabolic rate	8.5	14.1	4.9

(Omitting 9 cases because they do not follow the general trend of the readings)

	1.	2.	3.
Number of patients in group	21	21	21
Average number of days of pregnancy or puerperium	133	245	9
Average weight of patients (pounds)	126.54	144.07	126.1
Average basal metabolic rate	6.7	15.6	3.5

manifestation of an actual or a relative deficiency of iodine in the pregnant woman. The administration of small doses of iodine or the iodine-containing hormone, thyroxin, in the pregnant woman who develops even a slight enlargement of the thyroid or the one whose basal metabolism is far short of plus 15 per cent during the second half of pregnancy is, in my opinion, rational therapy.

The relatively low basal metabolic rate found at or near term in this series of cases is unique. Most investigators have found a much higher basal exchange during advanced pregnancy of normal women.

DR. PENDLETON TOMPKINS.—In looking over the statistics on the percentage of patients with enlargement of the thyroid during pregnancy, one finds a discrepancy of 40 per cent in Philadelphia and 80 per cent quoted by Murray and 60 per cent by Bloss. That difference can be explained by the difference in the probable iodine intake in those areas. As one passes farther and farther into the goiter belt, the incidence is higher.

Two groups of pregnant patients have been studied in parallel series, one receiving iodine as a matter of routine and one receiving none. I believe that in the group receiving iodine there were no hypertrophies and in the other there was the same percentage of hypertrophy as in the population in general. This supports Dr. Mazer's point.

A SUPERIMPOSED LIPEMIA DURING LABOR*

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IN SOME studies on the lipemia of pregnancy^{10, 15} analyses were made on blood taken at the end of parturition. There are a number of possible factors apart from pregnancy itself which conceivably might affect results obtained at that time. The anesthesia during delivery, the loss of blood, psychic disturbances, and labor itself are some of these. When values for blood lipids determined at the conclusion of labor are compared with values taken before labor¹ no marked differences are noted. For this reason no one has apparently considered the possibility that labor itself may affect blood lipid concentrations. In the present investigation, it was found that labor itself, when studied separately from the effect of the anesthesia and loss of blood during delivery, superimposes upon the lipemia of pregnancy a further lipemia. An indication that such was the case was revealed when by chance two samples of blood were taken from a parturient woman at different stages during labor.

Proceeding from this observation, 16 patients were studied from the Obstetrical Service of the Kingston General Hospital. A sample of blood was taken as soon as possible after the patient has gone into labor and a second sample just before administering anesthesia prior to delivery. There was necessarily considerable variation in the interval

*This work was aided financially by the Alice F. Richardson Fund of the Kingston General Hospital.

SUMMARY

The basal metabolic rate during normal pregnancy is increased above the normal for that particular patient and this reading (29 to 33 cases) is usually but not always, within the generally accepted limits of plus and minus 10. Occasionally an excitable patient had a basal metabolic rate higher than the average for this series. At the ninth lunar month the basal metabolic rate occasionally increased 33 points above the reading at the fifth lunar; generally it was only slightly elevated above the usual normal limits, but sometimes was a higher reading than expected. Occasionally the reading was lower at the second reading, thought due to an abnormal first reading at the fifth month. By the ninth day postpartum practically all basal metabolic rates (41 in 11 cases) were within normal limits and usually but not always somewhat below the level of the reading at the fifth lunar month. While no method was used to determine the cause of this slight increase in the basal metabolic rate, it is our impression that the cause is a combination of increased protoplasmic mass activating a slightly increased activity of the thyroid gland.

CONCLUSIONS

1. At the fifth lunar month of pregnancy, the basal metabolic rate is within normal limits (plus and minus 10).
2. At the ninth lunar month of pregnancy, the basal metabolic rate is slightly elevated (plus 14 to plus 16).
3. On the ninth day postpartum, the basal metabolic rate is again within normal limits, but usually slightly below the basal metabolic rate at the fifth lunar month.

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DISCUSSION

DR. CHARLES MAZER.—The conception of the mechanism of thyroid hyperplasia during pregnancy requires elucidation. It is not a physiologic manifestation to meet the need for thyroxin by the growing embryo, but rather a pathologic

The significant changes observed occurred only in plasma. In this part of blood, an increase was demonstrated in the majority of cases in all lipid values except those of ester cholesterol. The total lipid content of plasma increased during labor in 87 per cent of cases from an average initial value of 787 mg. per cent to a mean of 844 mg. per cent just before delivery. The mean increase of 57 mg. per cent had a standard deviation of 43 mg., indicating that in over 5 out of 6 cases one may expect an increase in total lipid during labor. The result was therefore statistically significant. The increases were slight. The mean increase in total lipid was but 7.3 per cent and the greatest increase was 14.2 per cent. During labor, thus, there occurs a superimposed lipemia which is not extensive but is consistent.

TABLE I. VARIATIONS IN THE LIPID CONTENT OF BLOOD DURING PARTURITION IN SIXTEEN PATIENTS.

VALUE	AVERAGE INITIAL VALUE (MG. %)	AVERAGE VALUE AT DELIVERY (MG. %)	AVERAGE CHANGE (MG. %)	STANDARD DEVIATION OF CHANGE (MG.)	NO. OF CASES SHOWING INCREASE (%)	AVERAGE PERCENTAGE CHANGE (%)
Blood Plasma						
Total lipid	787	844	+57	43	87	+7.3
Neutral fat	236	264	+28	27	62	+11.9
Total fatty acid	480	523	+43	30	94	+9.0
Total cholesterol	212	215	+3	25	62	+1.4
Ester cholesterol	140	135	-5	21	44	-3.6
Free cholesterol	72	80	+8	7	94	+11.1
Phospholipid	245	271	+26	17	100	+10.6
Red Blood Cells						
Total lipid	451	435	-16	21	44	-3.6
Neutral fat	61	52	-9	22	38	-14.7
Total fatty acid	247	237	-10	31	38	-4.1
Total cholesterol	112	112	0	11	50	0.0
Ester cholesterol	16	13	-3	9	19	-18.7
Free cholesterol	96	99	+3	6	69	+3.1
Phospholipid	268	268	0	22	44	0.0

The increase in total lipid was due to increases in neutral fat, free cholesterol, and phospholipid. In most lipemias such as those of normal pregnancy, diabetes mellitus, nephritis, and hypothyroidism, the lipid increased most in value is plasma neutral fat. On the average, neutral fat also increased more than any other lipid in the superimposed lipemia of labor. The relative increase in plasma neutral fat was not very much more than that of free cholesterol or phospholipid. There were more exceptions showing a slight decline in neutral fat values than in the case of the other two lipids. The fact that such decreases in plasma neutral fat were slight is seen from the mean changes and their standard deviation as shown in Table I. From this one may conclude that 5 out of 6 cases may be expected to show an increase in plasma neutral fat content during labor.

between samples. The shortest time was one and one-half hours and the longest was twenty-four hours. The average interval was ten hours and the median was eight hours. With an interval of less than two hours, the difference in lipid values of the two samples was slight. Between six and twenty-four hours, the differences in lipid values increased but very little with increase in the time. Hence, the superimposed lipemia of labor must occur largely in the last few hours of labor. When it was impossible to obtain the second sample of blood before giving anesthesia, the case was not included in the series. Anesthesia itself influences the concentration of blood lipids, affecting chiefly the red blood cells.

The anticoagulant used was heparin, in a concentration of 10 mg. per cent, because heparin has much less effect upon the partition of blood lipids than the anticoagulant salts. The first sample of blood was stored in the ice box until the second sample was ready and then both were centrifuged at full speed for one hour. It was found that no change occurred in the lipid values of heparinized blood stored for as long as three days in the ice box. Hence the differences observed in the lipid content between Samples 1 and 2 could not have been due to Sample 1 having stood longer than Sample 2. Plasma and red cells were extracted with 25 volumes of alcohol-ether, no heat being used,⁴ and the extracts were analyzed by the oxidative micromethods of Bloor as employed in previous investigations.¹⁻⁴

It was found impossible to insist upon fasting the patients previous to the withdrawal of blood. The diet of these women before their admission to hospital was unknown. In most instances the patients had been in labor some hours before admission and under such circumstances probably took little food. Certainly those in active labor had little taste for food until some hours after delivery. As emphasized in a previous communication,³ ordinary meals have practically no effect on the lipid content of blood of normal individuals but their effect on blood lipids of pregnant women is unknown.

Seven of the 16 women were primiparous and 11 were multiparous. Their ages varied between seventeen and thirty-eight years. No toxic signs or symptoms were evidenced by any of the cases.

RESULTS

The values determined by this differential lipid analysis included: total lipid, neutral fat, total fatty acids, phospholipid fatty acids, cholesterol ester fatty acids, neutral fat fatty acids, total cholesterol, ester cholesterol, free cholesterol and phospholipid. A total of 640 such values formed the basis of the present report. A statistical summary of these results is presented in Table I. The formula used for calculating the standard deviation of the mean has been previously given in this JOURNAL.²

Crampton¹⁴ attribute this to anoxemia plus other undetermined causes. Others¹² have suggested it is due to the effect of increased amounts of lactic acid in blood causing contraction of the spleen. There was no consistent change in the hemoglobin and red cell count in the present series of cases. In half of the cases they were increased and in half decreased during labor. In about two-thirds of the cases the percentage volume of the red cells rose during labor. There were insufficient cases to permit of a definite decision but the results suggested that possibly the volume of the red cells may increase during labor. This was not accompanied by any significant change in their lipid content.

SUMMARY

Heparinized blood was analyzed by oxidative micromethods and taken from 16 patients on two occasions, early and late in labor. It was found that during labor there occurred a significant increase in plasma phospholipid, free cholesterol and neutral fat with no change or a decrease in plasma ester cholesterol. There were no significant changes in the lipid content of the red blood cells. The results demonstrate the occurrence of a superimposed lipemia during labor which is probably due to muscular exercise.

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Vignes, H.: Pruritus Among Pregnant Women, Gynécologie 36: 88, 1937.

Vignes has observed 41 women who had vulvar and perivulvar pruritus during pregnancy and 15 women who had nonvulvar itching. These occurred in a series of 1,800 pregnant women. In 27 of the 41 cases there were no lesions but in the remaining 14 cases there were skin manifestations such as eczema, intertrigo, vulvitis, etc. Most of these patients reported that the pruritus began in the sixth month of pregnancy. In many cases, varicose veins were present and these were of etiologic significance. Six women had leucorrheal discharges. Vignes found that 19 women had definite evidence of syphilis, a few had hyperthyroidism, a few glycosuria, five had excessive vomiting or ptialism, three had psychic disturbances and three had pruritus after arsenic therapy. Treatment gave quick relief in most cases.

J. P. GREENHILL.

Values for plasma phospholipid showed the most consistent increase, this occurring in all of the cases. The greatest increase in phospholipid was 29 per cent and the least 1.8 per cent, the average increase being 10.6 per cent. Plasma free cholesterol values were raised relatively about the same extent as phospholipid and 15 of the 16 cases showed an increase.

Ester cholesterol of plasma fell in concentration during labor. A decrease in the ester cholesterol content while other plasma lipids are increasing has been previously noted in the lipemia of pregnancy in guinea pigs⁷ and in women⁹ and in nephritic lipemia.⁵ Boyd⁶ has described the interrelation of plasma lipid values with increasing total lipid and noted this eccentric change in ester cholesterol. Lipopenic variations in ester cholesterol have been missed apparently in less complete studies of other lipemias. Its significance is obscure. As a result, there was relatively little change in total cholesterol and the mean increase in total fatty acids was relatively less than that of phospholipid or of neutral fat.

On the average there occurred a decrease in the lipid content of the red blood cells during labor (Table I). In all instances, however, the standard deviation of the mean change was greater, and considerably greater, than the average change itself. This emphasizes that the changes were not consistent and this may also be seen in the column listing the number of cases showing an increase. In 81 per cent of cases there was a decrease in the ester cholesterol content of the red blood cells but all of these values were so low and the average loss so little that it is doubtful if the decrease be significant. One may conclude that the superimposed lipemia of labor is a phenomenon affecting plasma and not the red blood cells.

Of the various possible causes, muscular exercise would appear to be the most likely factor responsible for the superimposed lipemia of labor. Patterson¹³ showed that exercise produced a lipemia; Stewart, Gaddie and Dunlop¹⁶ confirmed this and noted that interrupted work periods produced a more marked lipemia. Fahrig and Wacker⁸ found that exercise increased cholesterol, cholesterol esters and "lecithin" as well as fat although others¹⁶ had noted an increase only in neutral fat. Houget¹¹ also noted a general increase in all lipids of blood following exercise in dogs. More strenuous exercise in the experiments of Stewart, Gaddie, and Dunlop¹⁶ would probably have resulted in a general rise in all blood lipid values rather than only in neutral fat as they found. By analogy, it would appear probable that the muscular exercise of labor is the factor responsible for the superimposed lipemia of labor.

Severe muscular exercise has frequently been found to produce an increase in blood hemoglobin and the red cell count. Schneider and

heard over the heart. No murmurs. *Abdomen*: no masses palpable. *Liver and Spleen*: not palpable. *Extremities*: nonpitting edema. Thick subcutaneous tissue. *Vaginal Examination*: excessive bleeding; *vagina* filled with clots. *Uterus*: no evidence of abortion.

LABORATORY DATA

May 9, 1936: *Urine* (chemical and microscopic) negative. Specific gravity, 1005 to 1013. *Blood*: R. B. C., 1,000,000. Hb, 58 per cent. W. B. C., 6,800. Neutrophile, 68 per cent. *Blood chemistry* (per 100 c.c. of blood): Chlorides, 479 mg. Cholesterol, 190 mg.

June 3, 1936 (after calcium therapy): Calcium, 9.6 mg. Phosphorus, 4.8 mg.

CLINICAL DATA

Temperature Range.—From 96° F. on admission to 104°. Elevated temperature subsided two days before onset of tetanic convulsions. Blood pressure: systolic 100 to 130; diastolic 60 to 92.

CONTINUATION NOTES

Immediate Therapy.—The usual operative gynecologic procedures in hemorrhage and its shock were instituted; however, bleeding promptly recurred, and on May 29, 2 c.c. of A.P.L. (Collip) were administered intramuscularly every eight hours; thyroid extract, 3 gr. t.i.d. for forty-eight hours, and then 1 gr. t.i.d. was ordered. Fluid intake of 5,500 c.c. with a urinary output of 2,600 c.c. Blood pressure (mm. of mercury): systolic 100; diastolic 60. *May 31*: excessive uterine bleeding controlled.

June 1, 1936: Tetanic convulsion, preceded by severe tetanic cramps and extremely painful flexions of thighs, knees, ankles, and toes.

Therapy.—Calcium gluconate (1 gram) intravenously. Morphine sulphate gr. $\frac{1}{4}$ and scopolamine gr. $\frac{1}{150}$. Calcium gluconate 1 gm. orally every 4 hours. Viosterol M XV daily.

June 3, 1937: Nausea and spasm of toes. Intravenous calcium gluconate, 1 gm., given.

Condition on Discharge.—No evidence of myxedematous swellings, and no vaginal bleeding for past eight days. Mentally bright. No signs or symptoms of tetany.

Therapy.—Thyroid, 2 gr. daily. Calcium chloride X gr. t.i.d. Viosterol XV M daily.

Bilateral partial thyroidectomy is the most frequent cause of parathyroid insufficiency and tetany; however, parathyroid tetany usually, but not always, occurs shortly after the thyroid operation. The onset of the tetany syndrome is rapid if the parathyroid glands are unintentionally removed, and latent if due to injury to the parathyroid tissues or their blood supply. The severity and duration of the symptoms depend upon the degree of the subnormal level of the blood calcium; convulsions usually occur when the calcium falls below 7.5 mg. per 100 c.c. of blood; the neuromuscular hyperirritability, spasms, Erb and Chvostek signs appear at the lesser subnormal blood calcium levels. Blood phosphorus rises as the blood calcium falls.

The parathyroids, the thyroid, and very likely, the anterior pituitary gland, are directly concerned in calcium metabolism and blood calcium.

Hyperthyroidism depletes the body calcium reserves and generalized osteoporosis frequently results; accordingly we feel that, exclusive of the factor of thyroid surgery, there are other factors responsible for the low blood calcium level and the tetanic syndrome: (1) lowered or depleted calcium stores due to the recent hyperthyroidism, (2) myxedema and the lack of thyroid mobilizing effect on calcium, and (3) lowered blood calcium level due to severe and prolonged hemorrhage.

MYXEDEMA WITH MENORRHAGIA AND TETANY AS COMPLICATIONS FOLLOWING A PARTIAL THYROIDECTOMY*

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THE purpose of this communication is to report a case of secondary postoperative parathyroid insufficiency, occurring in a negress, single, aged thirty-six years, who had a bilateral partial thyroidectomy three months prior to the onset of the menorrhagia and postoperative myxedema and the complication of tetanic convulsion and spasms.

Eason¹ in 1915 reported a case of myxedema with tetany, and Barker² cites that Frankl-Hochwart pointed out that struma was present in 13 of 26 cases of idiopathic tetany and mild myxedematous symptoms appeared in chronic tetany. In such cases, favorable results were obtained with thyroid extract on the trophic changes associated with tetany.

Pidoux,³ basing his opinion on his observations of six cases of parathyroid tetany in spontaneous myxedema (Pidoux, Eason, Lifschitz, Cantonnet, Morwitz, Kropeln) concludes that symptoms of parathyroid insufficiency may develop in myxedema or remain latent. The myxedema can be of congenital or acquired origin and has also been noted in Brissaud's infantilism.

Forsyth, quoted by Pidoux, observed changes in the parathyroid glands in a fatal case of myxedema. Engelbach,⁴ quoting various authors, states chronic tetany is likely to become acute in weak, anemic individuals, and tetany occurs during pregnancy as the result of severe hemorrhages and the loss of blood calcium, or when the increased calcium demands of the fetus are not met, due to the previously impaired parathyroid glands of the mother.

Kepler⁵ has observed tetany associated with myxedema but is of the opinion it is an infrequent complication of myxedema, and the literature on the subject supports this opinion.

CASE REPORT

J. S. was admitted on May 27, 1936, to the service of Dr. William R. Nicholson at the Graduate Hospital with the diagnosis of menorrhagia. *Previous illness:* syphilis (antisyphilitic therapy), appendectomy.

History of Present Illness.—Patient had bilateral partial thyroidectomy three months ago (Feb. 27, 1937) and was discharged in good condition with a basal metabolism rate of minus 15. On May 6, 1936, the regular menstrual period occurred; the flow was excessive (12 pads a day). Large clots were expelled and the period lasted for two weeks. Vaginal bleeding stopped for four days and reappeared three days ago. For twenty-four hours preceding admission to the hospital she had vaginal hemorrhage and extreme weakness.

Physical Examination (made by Resident Physician on admission).—The patient is extremely listless, in great contrast to the hyperthyroid patient of three months ago. She has gained over 30 pounds in three months, and is obese. *Skin and mucous membrane:* pale. *Pulse:* 75; *Respiration:* 20. *Temperature:* 96° F. *Blood pressure:* 130/80. *Scalp:* *Hair:* short and coarse. High forehead line. *Eye brows:* outer half very thin. *Face:* myxedematous appearance. *Skin and Scalp:* dry; generalized myxedema. *Speech:* thick; deep-toned. *Mental reactions:* sluggish. *Eyes:* moderate exophthalmus; pupils react to light and accommodation. *Ears and Nose:* negative. *Teeth:* dental caries. *Throat:* negative. *Cardiac:* only poor quality second sound

*Read before the Obstetrical Society of Philadelphia, May 6, 1937.

The postoperative period presenting negative evidence of parathyroid insufficiency, the case is best classified as a secondary postoperative parathyroid insufficiency because pathologic uterine bleeding due to the postoperative myxedema lowered the blood calcium, and since the parathyroids were incapable of elevating the blood calcium to normal, the tetanic syndrome occurred and the latent state of parathyroid insufficiency became apparent.

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DISCUSSION

DR. WILLIAM BATES.—The combination of factors in this case has proved quite interesting. Tetany due to injury or removal of parathyroid glands at the time of thyroid operations, occurs within six to eight hours after operation. In this case there was no such time relationship between partial thyroidectomy and the tetany seizures.

The only basal metabolic rate taken on the admission for hemorrhage showed a plus 18 to 23. This basal metabolism rate was taken on May 29, two days after admission, and after the administration of only 3 gr. of thyroid extract. There is no doubt in my mind that there are other factors than the thyroid function concerned with the rate. However, we apparently have here clinical evidence of deprivation of thyroid tissue and the tetany might be called thyroprival tetany which is a recognized classification.

There are several types of tetany encountered, such as rheumatic tetany, gastric tetany, hyperventilation tetany, latent tetany, parathyroid tetany, parathyroprival tetany, and thyroprival tetany.

However, until the calcium in circulation was depleted by hemorrhage, tetany did not occur in this case. Therefore, she is probably a potential parathyroprival or a potential thyroprival. By potential, I mean a type requiring some assisting factor, such as hemorrhage or other factors that lower blood calcium, to produce actual tetany. Therefore we are using the terms, secondary and potential, interchangeably, as meaning the need of assisting calcium depletion.

DR. DUNN (closing).—Yesterday a single girl of twenty-six years of age consulted me and gave the following history. In June, 1936, she had had a dilatation and curettage for severe hemorrhage. That was followed in ten days by laparotomy; part of the left ovary and half of the right ovary were removed. The hemorrhage recurred for thirteen weeks, and she was readmitted and dilatation and curettage were again performed which also did not stop the recurrent uterine hemorrhage, and dilatation and curettage and radium were given.

This girl had given a history of a basal metabolism of minus 20 for seven years. It was known in 1934 that she had a basal metabolism of minus 20. Thyroid was given, but because of a toxic reaction it was discontinued. Subsequently she had the above operations and the menorrhagia persisted.

I feel, as Gardner pointed out in his paper, the subject of hypothyroid menorrhagia is neglected. There is very little in the literature about thyroid therapy in the control of menorrhagias. Nothing will adequately control this girl's bleeding until she receives sufficient thyroid therapy.

It is our belief that in the case presented, the hemorrhage was the precipitating cause of the low blood calcium and the tetanic syndrome. The pulse of myxedema is bradycardic, therefore the pulse rate of 72 to 82 presents, at least, a 50 per cent increase in the abnormally low pulse rate, and is of a hemorrhage range and type.

The prompt disappearance of the tetany syndrome after the administration of calcium, as well as the posttherapeutic level of 9.6 mg. of calcium per 100 c.c. of blood, indicates the low pretherapeutic blood calcium level as the cause of the tetany.

With a history of bilateral partial thyroidectomy, and the above three factors directly affecting blood calcium metabolism and content, consideration of other clinical conditions causing tetanic spasms or convulsions appear unnecessary, since no diagnostic signs or symptoms exist which suggest their possible inclusion.

More important than the anatomic-pathologic diagnosis or clinical diagnosis is the therapy of menorrhagia as a symptom of myxedema. In 15 of the 59 cases studied by Gardner-Hill⁶ a major pelvic operation or x-ray therapy was resorted to for induction of artificial menopause to control the menorrhagia. These are major measures as compared to thyroid therapy, in menorrhagias of hypothyroid origin.

Early diagnosis of the hypothyroid menorrhagia is required because thyroid therapy has a distinct disadvantage as an emergency therapeutic agent. While intravenous thyroxin injection produces therapeutic effects earlier than oral therapy, still, ten days must pass before its full therapeutic effect is obtained. Thyroid extract requires even a longer period to act, consequently all forms of thyroid therapy in this and corresponding cases are of little value in the emergency control of the hemorrhage from a myxedematous uterus.

In this case, supplementing the gynecologic therapy, A.P.L. (Collip) was administered; 2 c.c. intramuscularly every eight hours for 4 doses. The bleeding was controlled in thirty-six hours. (We are indebted to Ayerst, McKenna and Harrison, Rouse's Point, N. Y., and Montreal, Canada, for the supply of Collip's A.P.L.)

Twelve hours later, a tetanic convulsion, preceded for a short time by cramps of the lower extremities, occurred, and 1/4 gr. of morphine sulphate, and 1/150 gr. of scopolamine. Orally 4 gm. of calcium gluconate was administered and 15 minims of viosterol daily. The tetanic convulsion was controlled by this therapy. A second intravenous calcium gluconate injection was given two days later when nausea and spasm of the toes appeared. The first blood calcium determination was reported on June 3, 1936, after calcium therapy had been started, and was 9.6 mg. calcium and 4.8 mg. phosphorus, and on this day the spasm of the toes reappeared, and intravenous calcium, 1 gm., was given.

The onset of the symptoms did not permit estimation of the blood calcium prior to the administration of calcium.

Under similar circumstances, should intravenous thyroxin be administered in preference to oral thyroid therapy? In this manner, earlier complete arrest of hemorrhage might be possible, however, over-effect of thyroxin is possible. Since the dosage of thyroxin must be estimated by basal metabolism rate determinations, the dosage of thyroxin in these circumstances must be empirical and lean to under-effect in preference to the possibility of causing hyperirritability from thyroxin nerve effect in a patient already having a supersensitive neuromuscular mechanism due to calcium deficiency. Under such conditions, oral therapy, which can be better controlled, seems advisable.

CONCLUSIONS

The menorrhagia, which was the first abnormal menstrual period, occurred three months after the bilateral partial thyroidectomy and coincident with the myxedematous state. The menorrhagia lasted fourteen days, ceased for four days, recurred and lasted five days more. The tetanic manifestations appeared twenty-four days after the onset of the menorrhagia, and three and one-half months after partial bilateral thyroidectomy.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Obstetrics

In response to an invitation from the publishers Weibel has undertaken the writing of two volumes, *Lehrbuch der Frauenheilkunde*,¹ the "healing art of women," a literal translation but a poor expression, on the combined study and practice of obstetrics and gynecology. He realizes the close intimacy of the two subjects, but does not avoid stating there are wide differences as well.

In this first volume, which deals mostly with obstetrics, he develops the sections on anatomy and physiology to cover all phases, bringing out the recent contributions on hormones. The discussion of normal pregnancy, diagnosis, physiology and hygiene is marked by its clarity and conciseness.

The mechanism of labor and its conduct are well presented. The sagittal section illustrations give an excellent portrayal of the processes involved in the various steps of delivery, and the serial roentgenographs of a spontaneous delivery, afford an excellent means of observing the attitudes of the fetus at different stages. The mechanism of the third stage is illustrated in a similar way, the placental vessels having been injected with an opaque substance. All the abnormal presentations are illustrated in a double manner, cut out section drawings and roentgenographs. This method of pictorial demonstration leaves almost nothing to be desired in the way of explanation.

In discussing anesthesia in labor, Weibel refers pointedly to the frequent disadvantages resulting, such as prolonged labor and enforced interference, as well as to the occasional danger of intrauterine death of the fetus when some of the recently proposed methods of amnesia are employed.

In discussing toxemias, hyperemesis gravidarum, the nephropathies as a group, and eclampsia are section titles. Weibel places all nonconvulsive toxemias under the second heading. He regards them as nephroses, though stating that an eclamptic convulsion may ensue if the condition progresses. Further stages he terms "eclampsism," then preeclampsia, and finally eclampsia. For the latter he recommends the conservative treatment of Stroganoff, although substituting sodium luminal for chloral hydrate.

There is a very fine discussion of the treatment of placenta previa; the different methods of delivery are fully dealt with in regard to the type of previa. Weibel appears to favor cesarean section, though he seldom expresses a very marked personal note in the text. While the pathologic aspect of puerperal sepsis is thoroughly presented, the outline of treatment is confusing. Weibel lists eleven drugs of proprietary type as of therapeutic value, but does not mention sulfanilamide.

The discussion of operative procedure is succinct and brief. The forceps of both Naegele and Kielland are discussed, the latter model is shown in all the illustrations of delivery by forceps.

¹*Lehrbuch der Frauenheilkunde* (in zwei Bänden). Von Professor Dr. W. Weibel, Vorstand der II. Universitäts-Frauenklinik in Wien. Erster Band: Geburtshilfe. Mit 849 zum Teil mehrfarbigen Abbildungen im Text und 16 farbigen Tafeln, 617 Seiten. Urban und Schwarzenberg, Wien, 1937.

A LATERAL VAGINAL WALL RETRACTOR*

MONTE C. PIPER, M.D., ROCHESTER, MINN.

(From the Section on Obstetrics and Gynecology, The Mayo Clinic)

RELAXED vaginal walls may be a detriment in applying the cautery to the uterine cervix because the lateral vaginal walls tend to fold between the blades of the ordinary speculum. These lateral walls not only obstruct the view of the cervix, but are likely to be touched by the shank of the cautery wire.

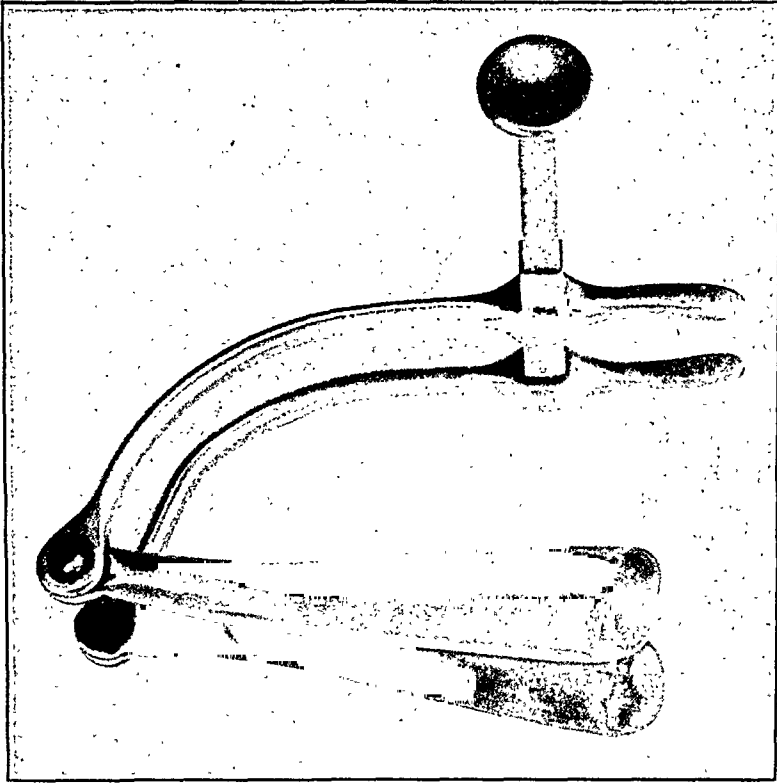


Fig. 1.—Lateral vaginal wall retractor.

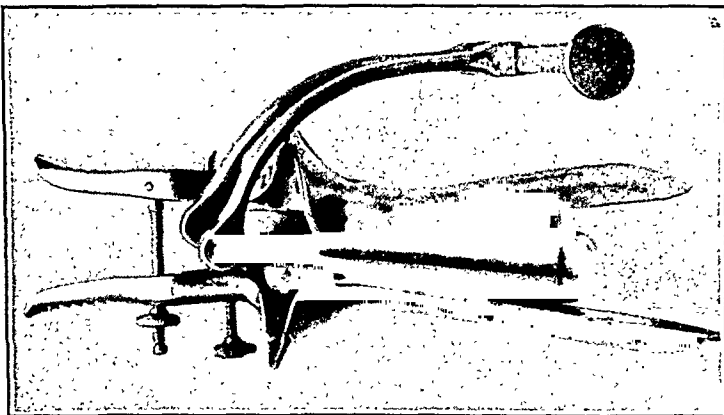


Fig. 2.—Blades of lateral vaginal wall retractor in place between blades of the speculum.

The lateral vaginal wall retractor assists in keeping the vagina adequately opened. It is placed in position after the speculum has been opened. The handles are hinged, so that they can be either elevated or depressed.

*Submitted for publication, January 2, 1937.

This instrument is manufactured by V. Mueller and Co., Chicago, Ill.

The author takes up again the subject of avoidance of infection, Chapter XXI, and reiterates and expands the details. Under anesthesia he says, "the most striking development in recent years, however, is the increasing favor with which spinal anesthesia is viewed." It is evident that Dr. Kerr also regards this method with favor. Chloroform is evidently the anesthetic of choice for house practice in the British Isles. Ten pages are devoted to amnesia and analgesia in labor. The subjects of version, forceps, mechanical enlargement of the pelvis, and cesarean section are comprehensively discussed, especially, in regard to the low segment operation with which the author's name is so intimately connected. Modifications, complications, and accessory operations in connection with cesarean section are described. There is ample description of the operative aspects of the various types of puerperal hemorrhages and the use of the blood transfusions is emphasized repeatedly in this connection. Separate sections are devoted to the traumatic conditions associated with operative delivery and obstetric shock, as well as to the injuries sustained by the child. Kerr, whose interest in maternal morbidity and mortality has led to a separate publication on that subject, quotes frequently on the statistical aspects of the morbidity and mortality attending the operative handling of abnormal labors.

This edition of Kerr's *Operative Obstetrics* is outstanding as a work of practical utility and as a reference book. It merits the highest praise.

—Philip F. Williams.

Brindeau and Lantuéjoul offer in *La Présentation Du Siège. La Version* an extended dissertation on the operative methods of delivery in a breech presentation, and also consider the technic of version. The book is divided in two parts, 75 pages of text, and 92 full page illustrations by Lemeunier.

The attitude of the authors toward this condition when discovered in pregnancy is one of laissez-faire. The authors feel that external version is difficult to accomplish in a primipara, and unnecessary in a multipara. The normal mechanism of breech is clearly described; the authors regard the breech as having three distinct phases, the pelvis, the shoulders, and the after-coming head, all of which should be considered in relation to the inlet, cavity, and outlet. Following very definite and conservative indications for interference, the generalities and the details of the technic of extraction are given. The method of Mauriceau is preferred to forceps in the usual run of cases. The difficulties encountered in extraction as well as the complications are well covered. Cesarean section in breech presentation is regarded as preferable to a difficult vaginal delivery, and may be indicated even after a trial labor. The relation of breech delivery to placenta previa is discussed. The authors conclude that a breech baby stands asphyxia better than traumatism, and that most complications are produced by the attendant.

The subject of version takes up both external and internal methods, and combined. Prophylactic version, "Méthode préconisée par les Américains," is rejected. The treatment of the subject is thorough and clear; particular stress is laid on the contraindications, dangers, and possible complications.

The ninety-two page illustrations by Lemeunier are beautifully executed. Many have from one to four insets showing details of a particular step in the operative procedure. Seemingly every possible complication and the appropriate maneuver are portrayed. The same may be said of the illustrations depicting version. There are included a number of roentgenographs or photographs of fetal injuries which may be sustained in the operations discussed.

This book with its complete discussion and superb illustrations is warmly commended.

—Philip F. Williams.

³*La Présentation Du Siège. La Version.* Par A. Brindeau, Professeur de Clinique Obstétricale et Gynécologique et P. Lantuéjoul, Accoucheur des Hôpitaux, Faculté de Médecine de Paris. Avec illustrations, PLXCII. Vigot Frères, éditeurs, Paris. 1937.

The book is profusely illustrated and the imprint is good, but the binding in paper is really worthless. The book serves as an example of present-day teaching and practice from the Vienna school, but lacks any personal note.

—Philip F. Williams.

On the foundation stones of his third edition of the textbook on *Operative Midwifery*, published in 1916, Dr. Kerr has erected a truly monumental textbook of *Operative Obstetrics*.² There are 832 pages of text and 338 illustrations. In the preparation of this fourth edition, the author has had the assistance of Dr. Donald McIntyre and Dr. D. F. Anderson. The American literature of recent years is widely quoted to so recent a time as within six months before publication.

The keynote of the present edition as in the previous one lies in the discussion of the knowing "when and how" to interfere. Particularly does Dr. Kerr stress the need for experience in obstetric surgery where the finesse and timing of intervention play so important a rôle.

Primarily, he discusses dystocia from the general aspects of the forces, the child and the passage, and the recognition of the early indications for interference. From this he passes to answering the question "how far can dystocia be prevented?" In elucidating the answer he presents chapters on obstetric diagnosis, radiography, examinations in labor, conduct of labor and the series of discussions on the prevention of infection, prevention of trauma and the subject of injury to the fetus.

After an analysis of the anomalies and faults in the forces, he passes on to the very detailed consideration of those instances, where, in labor, the cause of the dystocia can be found in the fetus. The treatment of occipitoposterior reflects the long experience of the author in abnormal obstetrics. He enumerates those symptoms and signs which are indicative of probable rotation and spontaneous delivery and those indicative of probable persistence of the posterior position. He attaches great importance to the manual correction of the shoulders as an aid in rotation. He feels that early conversion of the mentoposterior positions should be followed by successful delivery; for mentoposterior positions in the hands of the general practitioner he recommends version.

Kerr feels that all primigravidas with breech presentation should be confined in the hospital under the care of an expert operator. He regards external cephalic-version as the accepted treatment for breech presentations at the thirty-sixth week. The proposition of Burns and Marshall for the after-coming head should receive extended trial. Quoting figures on fetal mortality in breech presentations, the author states that the fetal death rate in this presentation should not be higher than four to six per cent in primiparas. There is an excellent discussion of oblique and transverse lies as well as of those due to congenital and anomalous conditions of the fetus, monsters, which in themselves cause dystocia. He recommends the wider use of radiography. The various complications of multiple births are discussed with the advice that the less interference the better.

The subject of dystocia due to contracted pelvis, and the many clinical and radiological methods of diagnosis are presented quite fully. There are many quotations from American authorities on this subject. Dystocia resulting from abnormalities affecting the soft parts, parturient canal, and its adjoined or adjacent structures is handled in the most comprehensive manner. The teaching for such conditions corresponds closely to the consensus of opinion in the United States.

²*Operative Obstetrics, A Guide to the Difficulties and Complications of Obstetric Practice.* By J. M. Munro Kerr, LL.D., M.D., F.C.O.G., Emeritus Regius Professor of Midwifery, University of Glasgow, Obstetric Surgeon, Glasgow Maternity Hospital. With the assistance of Donald McIntyre, M.D., F.C.O.G., Consulting Obstetric Surgeon, Barshaw Maternity Hospital and D. Fyfe Anderson, M.D., Senior Assistant to Professor of Obstetrics and Gynecology (Muirhead Chair) Glasgow University, With 338 Illustrations, William Wood and Company, Baltimore, 1937.

Included in *Leçons du Jeudi Soir à la Clinique Tarnier*⁸ are fourteen essays bearing on gynecology and obstetrics, which may be regarded as reflecting present-day French teaching and practice. Brindeau contributes a lengthy article on a genetic topic, "Congenital Hypognathism"; Ecalle has a meritorious contribution on the nonfebrile complications of the puerperium. Brouha discusses cancer of the cervix complicating pregnancy; he has observed three instances of this association recently. Among the remaining essays one must mention Gilbert's excellent discussion of roentgen therapy in myoma and Lantuéjoul's contribution on breech presentations in primiparas.

This year's papers compare most favorably with previous collections and sustain the high esteem in which the Clinic Tarnier is held in the obstetric world.

—Philip F. Williams.

Dr. Vaughan's interest in the sacrifice of life coincident with childbirth has caused her to make a wide study of the causes of difficulty in parturition. She has published the results of her inquiries in this book entitled, *Safe Childbirth: The Three Essentials; Round Brim, Flexible Joints, Natural Posture*,⁹ and concludes, as the title indicates, that these three essentials make for the safety of the mother and child. She discusses the problem of difficult childbirth particularly from the standpoint of mortality. Later in this part of the book she narrates the manner of care in delivery among the Andaman tribes, the various castes of Hindus and the countries of Europe.

She considers the cause of difficult childbirth to lie primarily in the unyielding pelvis, and states that the shape of the brim determines the capacity of the pelvis, and that a larger fetal head can be born through the pelvis with a circular brim than through any other shape of inlet of the same boundary measurements. She regards the pelvis with the circular brim as the only normal pelvis in women of all races. The most frequent alteration of the round pelvis she feels is the oval brim, and the etiology of this deviation is ascribed to bone disease, improper posture and absence of sunshine. It is asserted that a rough estimate of the pelvic shape and capacity can be predicated by the woman's shape and position of her teeth and jaws. The author discusses, and illustrates by roentgenographs, the influence of posture on the pelvic joints and pelvic measurements.

To obtain the normal pelvis as described by Dr. Vaughan it is necessary to begin with intrauterine life, and after birth to follow the child through infancy and adolescence constantly overseeing the diet and posture.

Finally, when parturition ensues in a woman so cared for, she should be allowed to adopt the squatting position and other postures commonly used among primitives. The author narrates experiences with a group of women who practiced exercises during the pregnancy to enlarge the pelvic joints, and in labor used the postures suggested.

In concluding this review, a sentence from the foreword, written by Dr. Howard A. Kelly, may be quoted, "Whether all the doctor's conclusions are at once accepted or not, it is of vital importance that they be most carefully considered and duly weighed."

—Philip F. Williams.

⁸*Leçons du Jeudi Soir à la Clinique Tarnier*. Avec 70 figures. Vigot Frères, éditeurs, Paris, 1937.

⁹*Safe Childbirth. The Three Essentials*. By Kathleen Olga Vaughan, formerly Medical Officer, Egyptian Quarantine, etc. With foreword by Howard A. Kelly. Illustrated, 154 pages. William Wood and Company, Baltimore, 1937.

Vignes has withdrawn for separate publication his article on the physiology of *Gestation*⁴ which appeared in the second edition of the textbook on physiology edited by Roger and Binet. In this section he has developed the material under three rubrics: the physiology of the embryo and fetus, physiology of the placenta and membranes, and the modifications and alterations of function experienced by the pregnant organism. With graphs, charts, and tables he illustrates the growth and development of the child, and its constituents of a mineral nature. He remarks particularly on the inconstancy of the accepted signs of fetal maturity. In discussing immunizing substances, he feels that the complement content of the fetal blood is nil or very little, and that what immunity the newborn child has is a passive one. He feels that it is possible for an antigen to traverse the placenta. He regards the blood of the newborn as not being separable into groups. There is an excellent discussion of the interrelationship of the fetal pancreas and maternal blood sugar, especially if diabetes exists in the woman.

The physiology of the placenta in the light of recent researches is fairly discussed, and the author develops at length the newer physiology of pregnancy in regard to the glands of internal secretion, as well as giving very complete dissertations on the physiology of the other systems.

—Philip F. Williams.

This book, *Maladies des Femmes Enceintes, Affections des Muqueuses Génitales*,⁵ forms the fourth of a series of monographs on the complications of pregnancy.

In this volume Vignes discusses at length the diseases of the cervix, vagina, and vulva. The various infections, infestations and newgrowths of these three areas are described and discussed, not alone from the standpoint of pathology and therapeutics, but upon their relation to the physiology and pathology of pregnancy.

The subject of trichomonas infestation occupies eight pages of text, which offers an idea of the comprehensive manner in which the various topics are discussed. This is an excellent reference book, with a very large bibliographic reference index.

—Philip F. Williams.

In this *Maladies des Femmes Enceintes, Affections de la Peau*,⁶ the third in a series of monographs discussing the systemic complications of pregnancy, Vignes particularizes on the lesions of the skin. The text shows that a wide review of the literature has been made and the subject matter covers the entire field of cutaneous medicine. This book forms an excellent reference volume.

—Philip F. Williams.

Vignes⁷ offers a well-arranged bibliography of his surprisingly numerous contributions to all branches of obstetrics, gynecology, and other subjects. There are more than 700 titles in which are included numerous books. Both clinical and laboratory investigations have been performed by this very fecund author whose style is most readable, whose search of the literature is minute and whose breadth of knowledge is amazing.

—R. T. Frank.

⁴La Gestation. Par H. Vignes. 211 pages. Masson et Cie, Paris, 1936.

⁵Maladies des Femmes Enceintes, IV, Affections des Muqueuses Génitales. Par Henri Vignes, Professeur agrégé à la Faculté de Médecine, Accoucheur des Hôpitaux de Paris, Masson et Cie, Paris, 1937.

⁶Maladies des Femmes Enceintes, Affections de la Peau. Par Henri Vignes, Professeur agrégé à la Faculté de Médecine, Accoucheur des Hôpitaux de Paris, Masson et Cie, Paris, 1937.

⁷Exposé des Titres et des Travaux Scientifiques. By Dr. H. Vignes. 197 pages. Masson et Cie, Paris, 1937.

This delightfully fascinating story of childbirth, *Into This Universe*,¹² has evidently been prepared for laymen but all physicians will find Dr. Guttmacher's story of intriguing interest and well worth reading.

The imaginative recital of Ambroise Paré and his version on Marguerite de Puis in the sixteenth century, is an epic. It signalizes the beautiful manner with which Dr. Guttmacher has traveled through the obstetric folk-lore of the ages, with wide ranges in the literature of both lay and medical sources of different epochs and countries, to illustrate the history of childbirth. And so through the problems of the diagnosis of pregnancy, the physician's observations and the modern laboratory tests, we find a continuing recital of the development of modern science. In the section on pregnancy, the lay person will find not only an explosion of the theory of maternal impressions, but a safe and sane exposition of the principles of present-day prenatal care.

The story of labor, written in a fully explanatory manner, should in no sense alarm any woman who might read the chapters, but should convey to her a complete yet reassuring explanation of what actually happens when a baby is born, even to the discussion of the obstetric operations. In a like manner the subject of the puerperium and the newborn child is discussed. In marked contrast to the not infrequent diatribes on maternal mortality in lay journals is the exceedingly sane, although frank, discussion of morbidity and mortality in the chapter entitled "Safer Childbirth."

We may all hope with Dr. Guttmacher that, with study and progress, the many problems of obstetrics may soon be solved. The documentation of the book is thorough, and the list of contributions and books in the bibliography should be of interest to all who wish to read further in this story of childbirth.

—Philip F. Williams.

In this historical chronicle, *Childbirth: Yesterday and Today*,¹³ Dr. Rongy describes the attitude of various peoples and ages toward maternity. This fascinating story is presented in simple language and should be of interest as much to physicians as to the public, for whom it seems to have been intended.

Primitive practices and customs among the Orientals and later the Greek and Roman peoples evidence how long this natural function has been shrouded in mystery and ignorance. Rongy describes the early awakening of scientific medicine in the fifteenth and sixteenth centuries and explains how these advances were soon reflected in obstetrics. There is an interesting account of the early operative developments in obstetrics, including the story of the Chamberlen family and their forceps.

He passes on to the work of Holmes and Semmelweis, Gordon and White, and stresses the point that puerperal sepsis is still the great cause of death in the parturient. The development, place in society, and present status of the midwife forms an interesting chapter. Rongy points to the gradual elimination of this factor in obstetric work. In discussing child care and the methods used among many people he shows the gradual influence of the development of scientific medicine. He brings in chapters on the mystery of birth, and the place of the father as regards delivery among different peoples. He relates that birth control was the practice among both the ancient Hebrews and Greeks and comments on the continuance of this practice in our modern times. He feels that, ultimately, contraceptive birth control will be legally sanctioned. Finally, he discusses the modern practice of obstetrics with its overspecialization, and, as far as the United States is concerned, the factors bearing on the high maternal mortality rate.

¹²*Into This Universe. The Story of Human Birth.* By Alan Frank Guttmacher, Associate in Obstetrics, Johns Hopkins University, Illustrated, 366 pages. The Viking Press, New York, 1937.

¹³*Childbirth: Yesterday and Today.* By A. J. Rongy, M.D., Attending Obstetrician and Gynecologist, Lebanon Hospital, etc. With 20 illustrations, 192 pages. Emerson Books, Inc., New York, 1937.

The late George Davis Bivin, who was particularly interested in the prophylaxis of psychoneurosis and psychoses in children, had in the course of his researches become interested in the subject of *Pseudocyesis*,¹⁰ and had collected a great amount of material on this subject previous to his death. This material has been edited by his associate, Miss Klinger. The early conception of this condition held by Bivin is that it should be looked upon as a conversion hysteria, a functional disturbance. Later, he formulated the hypothesis that pseudopregnancy, a normal state in the menstrual cycle, becomes pseudocyesis, an abnormal state, because the hormones which regulate this phenomenon are thrown out of balance by physical or emotional changes, or a combination of these two factors. Since he drew no conclusions regarding his theories, this material has not been incorporated in this work.

Miss Klinger presents an analysis of the cases studied, which represent an enormous collection of references to this condition. The literature was reviewed as far back as 1721 at which time an article by Mauriceau appeared. Every symptom in each case, which the reporting physician had specifically mentioned, is tabulated. In the chapter on symptomatology the occurrence and disturbance of these symptoms is discussed. In the order of relative frequency, with which the various organs or physical conditions were mentioned, it is noted that the menstrual changes had a relative frequency of 100, abdominal changes of 99, breast changes 93, fetal signs 79, uterine contractions 50. The comments of the reporters of these various cases on diagnosis form the text of the succeeding chapter. Miss Klinger gives an interesting historic résumé of the etiologic theories beginning with the observation of Hippocrates, continuing with those of Mauriceau, Parvin, Mitchell, and Liepmann, the latter developed a threefold cause which he based in part on Pavlov's experiments. Further, she discusses the reason for certain specific symptoms as interpreted from the reported cases. Among the therapeutic measures employed there are included twelve instances where curettage was used and ten instances where surgery of the pelvic organs was performed. In a number of cases treatment was accomplished by insertion of a catheter in the bladder.

Miss Klinger concludes that pseudocyesis is a psychoneurotic condition probably best classified as an hysteria, for which the most successful treatment is destroying the patient's conviction of her pregnancy. The bibliography of case reports takes up fifteen pages.

—Philip F. Williams.

In a preceding publication Nevinny had advanced valid proof that such mechanical factors as venous stasis definitely play a rôle in the actual causation of certain types of cerebral birth injuries. Such stasis as a rule is due to a state of intrauterine asphyxia. In this study entitled *Medicamentous Relief of Intrauterine Asphyxia*¹¹ Nevinny presents conclusions based on experimental investigations and clinical observations. Inhalation anesthesia can relieve fetal asphyxia caused by exaggerated uterine activity, ether in this respect offering certain advantages over chloroform. However, in a larger number of instances fetal heart action more effectively is improved by drugs directly influencing circulation, especially by Cardiazol. This drug also seems to prevent uterine overactivity. It proves useful in strengthening fetal cardiac action preceding operations, thus reducing the harmful effect if operative intervention on the child is required.

—Hugo Ehrenfest.

¹⁰*Pseudocyesis*. By George Davis Bivin, Ph.D. and M. Pauline Klinger, M.A. The Principia Press, Inc. Bloomington, Indiana, 1937.

¹¹*Medikamentöse Bekämpfung der Intrauterinen Asphyxie*. Von Dr. med. habil. H. Nevinny, Universitäts-Frauenklinik, Königsberg. Pr. Mit 48 Textabbildungen, 104 Seiten. Ferdinand Enke, Stuttgart, 1937.

So in this book are assembled ample instruction on the theory and practice of both branches, as well as specialized information for the institutional nurse working under organized systems, the family nurse serving the general practitioner in home practice, as well as the needs of the public health nurse either on urban or rural assignments.

The material on obstetrics is presented in a simple, easily understandable manner, and with a logical sequence of subjects. It is very possible that there is a slight overbalance at times, as for instance, the space devoted to the mutilating operation on the fetus. Two sections are worthy of special notice, the chapter on the outpatient nursing services and that on the nurse in the home delivery. If in the latter situation a capable nurse is cooperating with the physician, it is a blessing and benefit. The section on gynecology and gynecologic nursing leaves little to be desired. The theory is short, concise, and medically authentic. The nursing procedures detailed and discussed are those of particular use in the surgery or treatment of pelvic lesions.

—Philip F. Williams.

In preparing the present eleventh edition of his *Obstetrics for Nurses*¹⁸ DeLee has obtained collaboration of Mabel C. Carmon, R.N., and her name appears as co-author. This book has been so favorably received over a period of thirty-three years that an extended review seems unnecessary.

The chapter on hospital obstetrics has been rewritten by the co-author, to present a fuller consideration of institutional technic, while new material has been introduced in various other chapters. The chapter on hospital obstetrics is, in miniature, a very complete manual of the care of the parturient woman from her admission in labor until she is sent to her ward or private bed.

The duties of the personnel, the preparation of material used, the set up of instrument trays for normal and operative deliveries, and the administration of medicine are detailed. DeLee suggests the use of palm prints on dactyloscript as a more permanent means of identification of the newborn infant than sole prints.

There is every evidence that the present edition will maintain the long and well-deserved popularity of its predecessors.

—Philip F. Williams.

This little book is written by a man of experience in country practice from a town with a population of eleven thousand. This *Physicians' Guide Book for Mothers*¹⁹ gives a simple and concise set of directions as to prenatal care and care after delivery. The third chapter discusses the final examination after delivery, which he might possibly term the follow-up examination. He adds some very pertinent observations of the necessity of the cooperation of the public with the physician in maternity work, and stresses the danger signals of complications which may arise in pregnancy or the puerperium.

On the title page are entries of the woman's name and address. The appendices include perforated pages for the physician to fill out and upon which he may note the prenatal and delivery record. An omission is that the pelvic measurements are not listed. Following the weight record of the mother are pages upon which special directions, notations for supplies and questions on the care of the mother and the baby may be entered.

¹⁸*Obstetrics for Nurses*. By J. B. DeLee, A.M., M.D., Professor of Obstetrics and Gynecology, Emeritus, University of Chicago, Consultant in Obstetrics, Chicago Lying-In Hospital and Dispensary; Consultant in Obstetrics, Chicago Maternity Center, and Mabel C. Carmon, R.N., Chief Supervisor and Instructor in the Birth-rooms, Chicago Lying-In Hospital and Dispensary. Eleventh Edition with 291 illustrations, 659 pages. W. B. Saunders Company, Philadelphia and London, 1937.

¹⁹*Physicians' Guide Book for Mothers*. By G. G. Keener, M.D. Southern Publishers, Inc. Kingsport, Tenn., 1936.

As stated above, this delightfully written historical account of obstetrics should be of value not only to the lay person but to the physician as well.

—Philip F. Williams.

In this small volume, *Safely Through Childbirth*,¹⁴ Dr. Rongy describes the story of pregnancy and childbirth for the lay audience in the hope that it will contribute to a greater understanding of this fundamental aspect of science.

Simply, but clearly, he discusses anatomy, conception, and the physiology of pregnancy. There is a very sane discussion, useful for doctors as well as the laity, of relief of pain in labor. The section on prenatal care, although short, is quite thorough. The various types of operative deliveries are briefly touched upon. Dr. Rongy missed an excellent opportunity to do a little missionary work when he failed to discuss criminal abortion, and its often tragic consequences. A philosophic description of the menopause completes the work. This book is well suited for lay education in obstetrics.

—Philip F. Williams.

The widespread campaign for the improvement of *Maternal Care*¹⁵ showed a need for the concise statement of the principles of antepartum, intrapartum, and postpartum care. It is felt that this handbook prepared by a group of members of the American Committee on Maternal Welfare will amply supply the needs of the average practitioner of obstetrics. The material is simply and directly presented with emphasis on the cardinal principles and insistence on the nearest approach to asepsis which is possible, and a short and direct discussion of obstetric operations and complications.

It is hoped that this handbook will have a wide distribution among general practitioners, hospital internes, and public health nurses.

—Philip F. Williams.

The 1936 report of the *Obstetric Clinic of the Hospital of San Juan de Dios*¹⁶ of which the chief is Professor Del C. Acosta, is submitted. This covers a report of 1,846 patients. In addition to the statistics, it contains a number of papers on various subjects, mainly clinical, such as tumors in pregnancy, anesthesia, the treatment of septic abortion by means of sera, and a casuistic such as two cases of infected fibroids during the puerperium. Judging by this report, syphilis is very prevalent among pregnant women in Colombia.

—R. T. Frank.

For the first time, as far as we are aware, the subjects of *Obstetric and Gynecologic Nursing*¹⁷ have been combined in one book. In recognition of the changing trends in nursing education the authors, Dr. Falls and Miss McLaughlin, have written this book to encompass the varying situations in which obstetric, as well as gynecologic, nursing finds a field.

¹⁴*Safely Through Childbirth*. By A. J. Rongy, Attending Obstetrician and Gynecologist, Lebanon Hospital, etc. With 20 illustrations, 192 pages. Emerson Books, Inc., New York, 1937.

¹⁵*Maternal Care*. The Principles of Antepartum, Intrapartum, and Postpartum Care for the Practitioner of Obstetrics. Approved by the Committee on Maternal Welfare, Inc. By Dr. Fred L. Adair, Editor. The University of Chicago Press, Chicago, Ill.

¹⁶*Boletín Anual 1936*. *Clinica Obstetrica, Hospital de San Juan de Dios*. Bogota, Colombia.

¹⁷*Obstetric and Gynecologic Nursing*. By Frederick H. Falls, M.D., Professor of Obstetrics and Gynecology, University of Illinois, College of Medicine, etc. and Jane R. McLaughlin, Supervisor of the Department of Obstetrics and Gynecology, Research and Educational Hospital, etc. With 83 illustrations, 492 pages. The C. V. Mosby Company, St. Louis, 1937.

clusions in regard to causative factors harmonize well with those announced by other writers. Of special interest, however, is the emphasis he lays on the possible prevention of intrauterine asphyxiation by two means, readily available, namely, administration of the cardiac stimulant cardiazol, or slight inhalation anesthesia when uterine contractions are severe or follow each other too quickly. He feels certain that in this manner many infants can be protected against cerebral injuries. It seems superfluous to add that the diagnosis of injury to the central nervous system can be made or excluded only if the autopsy is extended to a study of the spinal cord throughout its entire length.

—Hugo Ehrenfest.

Torild Brander from Finland has written a monograph on the *Development of Intelligence in Premature Children*.³⁴ These children were investigated between the seventh and fifteenth year from both a physical as well as a neuropsychical point of view. Such a study will probably be feasible only in small countries where the population is sessile.

Where the birth weight was under 2,500 gm. the case was classified as premature. Previously investigators used various criteria. If the I.Q. is employed, more defectives are noted. His material was based on 18,000 births of which 12.8 per cent were premature, a total of 2310. Of these, 1240 died before the mother was discharged from the clinic, 1070 children being discharged. Of these, 240 died subsequently; 583 were found alive in the age period of seven to fifteen years.

The Binet-Simon-Terman tests were employed throughout; 376 cases could be examined. Of these, 86 were twins, 22.9 per cent. Of the twins (42 pairs), 11 twins showed weakmindedness, 22.6 per cent. Of 290 single births, 31 or 10.7 per cent showed weakmindedness. Of all the children examined, 46 per cent were found normal in intelligence, 56.7 per cent below standard, 1.4 above standard, and 11.2 per cent distinctly weakminded.

Birth weights between 1,000 and 1,500 did not show a single normal child. Complications during labor increased the percentage of mental defectives. Children from low social groups showed a depressed I.Q. In the general population 12.5 to 25 per cent of all mental deficiencies are ascribed to premature birth. An interesting casuistic section and a number of illustrations add further value to this important contribution.

—R. T. Frank.

In this little monograph, *Unreife und Lebensschwache*,³⁵ Peiper presents the story of the premature and immature baby. He notes that from 5 to 10 per cent of births fall in this class, of whom less than half reached the end of the first year of life. Regarding cause of such births it is noted, that in three very large series, the cause was undetermined in an average of 48 per cent, while syphilis, the next largest cause after multiple pregnancy, averaged 7.5 per cent. Various sections discuss weight, chemical values, hormone production and ferment content, physiologic manifestations, and cerebral deviations. External influences in development as nursing, infection, nutrition, are considered. Peiper regards a birth weight of 2,000 gm. as the basic limit for organic dysfunction. This monograph should be of interest to those concerned with the scientific aspects of the problem of immaturity.

—Philip F. Williams.

³⁴Studien Ueber Die Entwicklung Der Intelligenz Bei Fruehge borenen Kindern. Von Torild Brander. Mit 58 Abbildungen und 67 Tabellen nebst tabellarischen Beilagen. Helsingfors, 1936.

³⁵Unreife und Lebensschwache. Von Professor Dr. Albrecht Peiper, Wuppertal. Mit 10 Abbildungen, 103 Seiten. Verlag von Georg Thieme, Leipzig, 1937.

It might be well that some of the Social Security funds devoted to maternal welfare be used in distributing samples of this book throughout the rural areas of the United States.

—Philip F. Williams.

This fine book, *Getting Ready to Be a Mother*,²⁰ by Miss van Blarcom has reached its third edition. In this edition new material on habit training and other topics has been added. The first half of the text is a well-considered presentation of prenatal care and of preparation for labor.

The second half is an excellent manual on baby care in all its multitudinous details. Several appendices describe the physiology of reproduction. The language used is clear and concise, the statements made are direct and medically correct. One feels that the average woman who is getting ready to become a mother will get much help from reading this book, and incidentally will be likely to cooperate more fully with her medical attendant.

—Philip F. Williams.

Newborn, Infants, and Children

Tow's *Diseases of the Newborn*²² is designed mainly for the general practitioner but should be of interest to the pediatrician as well. It deals with the first month of life. There is much valuable data in the chapter on general considerations. The author advises intramuscular injection of camphor in oil to inhibit lactation in the mother. For pylorospasm, atropine, phenobarbital and calcium are indicated. Any newborn infant under 5 pounds in weight is considered premature. Treatment in this group has little effect on the number of deaths occurring within forty-eight hours postpartum.

In the chapter on birth injuries, it is stated that the majority of diplegias are due to the pathologic process of intrauterine origin. By no means will all obstetricians agree with this point of view. The disorders of the various systems are taken up in order, the skeletal, the genitourinary, the nervous system; then eye, ear and nose; and finally the septic and infectious diseases.

Of particular interest to the gynecologist are the cases and references under female genital tract. For example, a case of prolapse of the uterus at birth combined with other deformities; mixed tumors of the vagina and similar genital disturbances noted at birth.

Whether such a statement as "an equable state of mind on the part of the mother is the most important single factor in the production of good breast milk" can be accepted in view of our present endocrine knowledge is more than doubtful. The book is well written, and each chapter concludes with a good bibliography.

—R. T. Frank.

*Birth Injuries of the Central Nervous System*²³ are thoroughly discussed by H. Nevinny in this small monograph. After surveying the very extensive literature on the subject the author analyses in detail a comparatively large material consisting of 153 cases that have been autopsied. In general, his findings and con-

²⁰*Getting Ready to Be a Mother.* By Carolyn Conant van Blarcom, R.N. Third edition, revised. With 97 illustrations, 305 pages. The Macmillan Company, New York, 1937.

²²*Diseases of the Newborn.* By Abraham Tow, M.D., Adjunct Professor of Pediatrics, New York Polyclinic Hospital, etc. Illustrated, 477 pages. Oxford University Press, New York, 1937.

²³*Die Geburtstraumatischen Schädigungen Des Zentralnervensystems.* Von Dr. Med. H. Nevinny, Universitäts-Frauenklinik in Königsberg, Pr. Mit 8 Textabbildungen und 12 Tabellen. 87 Seiten. Ferdinand Enke, Stuttgart, 1936.

American Association of Obstetricians, Gynecologists, and Abdominal Surgeons Annual Prize

The American Association of Obstetricians, Gynecologists, and Abdominal Surgeons has recently announced a new annual prize of \$500.00. Those eligible include only (1) internes, residents, or graduate students in obstetrics, gynecology, and abdominal surgery, and (2) physicians (M.D. degree) who are actually practicing or teaching obstetrics, gynecology, or abdominal surgery.

Competing manuscripts must (1) be presented in triplicate under a *nom-de-plume* to the Secretary of the Association before June 1, (2) be limited to 5,000 words and such illustrations as are necessary for a clear exposition of the thesis, and (3) be typewritten (double-spaced) on one side of the sheets, with ample margins.

The successful thesis must be presented at the next annual (September) meeting of the Association, without expense to the Association and in conformity with its regulations.

For further details, address Dr. James R. Bloss, Secretary, 418 11th Street, Huntington, West Virginia.

Officers of American Association of Obstetricians, Gynecologists and Abdominal Surgeons

The following Officers were elected at the annual meeting held in September, 1937:

President—Dr. Paul Titus, Pittsburgh, Pa.

President-Elect—Dr. James E. King, Buffalo, N. Y.

Vice President—Dr. Albert Mathieu, Portland, Ore.

Secretary—Dr. James R. Bloss, Huntington, W. Va.

Assistant Secretary—Dr. LeRoy A. Calkins, Kansas City, Mo.

Treasurer—Dr. Lewis F. Smead, Toledo, Ohio.

Members of the Council for three years:

Drs. James W. Kennedy, Philadelphia, Pa., and W. Wayne Babcock, Philadelphia, Pa.

International Congress of Obstetrics and Gynecology Amsterdam, May 4 to 8, 1938

Under the Patronage of H. M. the Queen of the Netherlands

Honorary Chairmen

Dr. H. Colijn, Prime Minister and Minister of Foreign Affairs.

Prof. Dr. J. S. Slotemaker de Bruïne, Minister of Public Institution.

Mr. Dr. A. Baron Röell, Governor of the Province of Noord-Holland.

Dr. W. de Vlugt, Burgomaster of Amsterdam.

The necessity for another edition of *Diseases of Infants and Children*³⁶ gave Griffith and Mitchell an opportunity to make many important changes in this volume, which had met with universal and prompt approval at the time of its appearance. Much new material has been added in the chapters dealing with anatomy, physiology, and growth of the newborn and young infant, artificial feeding, disturbances of acid-base balance, dehydration, and many other conditions. We mention the foregoing topics in particular because we feel that every physician doing obstetric work of necessity must be informed on these aspects of pediatrics and because we know of no other textbook which deals with the entire subject better than this volume.

—Hugo Ehrenfest.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MAY 6, 1937

The following papers were presented:

The Management of Pregnancy and Labor Complicated by Triplets. Dr. John C. Hirst. (This article will appear in a later issue.)

Myxedema With Menorrhagia and Tetany as Complications Following a Partial Thyroidectomy. Dr. Charles W. Dunn, and Dr. William R. Nicholson. (For original article, see page 164.)

The Basal Metabolic Rate in Normal Pregnancy. Dr. George C. Hanna, Jr. (For original article, see page 155.)

Items

American Board of Obstetrics and Gynecology

The next examination (written and review of case histories) for Group B candidates who have filed applications will be held in various cities of the United States and Canada, on Saturday, February 5, 1938.

The general oral, clinical and pathological examinations for all candidates (Groups A and B) will be conducted by the entire Board, meeting in San Francisco, California, on June 13 and 14, 1938, immediately prior to the meeting of the American Medical Association.

Applications for admission to the June, 1938, Group A examinations must be on an official application form and filed in the Secretary's Office before April 1, 1938.

For further information and application blanks address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pa.

³⁶The *Diseases of Infants and Children*. By J. P. Crozer Griffith, Emerit. Professor of Pediatrics, University of Pennsylvania, etc. and A. Graeme Mitchell, Professor of Pediatrics, College of Medicine, University of Cincinnati, etc. Second edition, revised and reset. 1154 pages. W. B. Saunders Co., Philadelphia, 1937.

American Board of Obstetrics and Gynecology

LIST OF DIPLOMATES LIMITING THEIR PRACTICE TO OBSTETRICS AND/OR GYNECOLOGY

TO DATE, JANUARY 1, 1938

Alabama

Birmingham

DOUGLAS, G. F.
GARRISON, J. E.

Arizona

Phoenix

BROWN, P. T.

Arkansas

Little Rock

HINKLE, S. B.

California

Alhambra

COLEMAN, D. D.

Berkeley

PAGE, C. W.

Glendale

MARSHALL, HAROLD K.

Los Angeles

ABRAMSON, M. J.
AINLEY, F. C.
FALLAS, R. E.
FIST, H. S.
GREENBAUM, G. B.
HANLEY, B. J.
IRWIN, J. C.
JOHNSON, O. D.
KRAHULIK, E. J.
LAZARD, E. M.
MCBURNEY, R. D.
MCNEILE, L. G.
PIERCE, S. N.
ROONEY, H. M.
ROSS, M. H.
SALISBURY, C. S.
SHAW, H. N.
SLEMONS, J. M.
THOMPSON, W. B.
TIBER, L. J.
TOLLEFSON, D. G.
VRUWINK, JOHN
WILLIAMS, N. H.

Oakland

BELL, T. F.
EWER, J. N.
LOOMIS, F. M.
SHERRICK, J. W.

Sacramento

KANNER, H. M.

San Diego

McGEE, W. B.
*NEWMAN, H. P.

San Francisco

BERNSTEIN, ABRAHAM
CRAIG, R. G.
DeCARLE, D. W.
DUNN, ROBERT D.

EMGE, L. A.

FLUHMAN, C. F.

LYNCH, F. W.

MAXWELL, ALICE F.

MOORE, W. G.

PETTIT, A. V.

SPALDING, A. B.

STEPHENSON, H. A.

VOLLMER, A. M.

San Jose

SHUFELT, A. A.

San Mateo

HOLMES, O. M.

Santa Barbara

NICHOLAS, CONSTANTINE
Z.

Santa Monica

LEWIS, C. H.

Colorado

Denver

INGRAHAM, C. B.
MASON, LYMAN W.
POWELL, CUTHBERT
WEINER, MORRIS

Connecticut

Bridgeport

HOWARD, J. H.

Hartford

COGAN, G. E.
MILLER, J. R.
STORRS, R. W.
THOMPSON, H. G.

New Haven

*HERSHMAN, A. A.
LEWIS, R. M.
MORSE, A. H.
MUSSELMAN, LUTHER K.
PERRINS, H. B.
STONE, EMERSON L.
THOMS, HERBERT

Norwalk

WALLACE, VICTOR G. H.

Stamford

WALLACE, VICTOR, G. H.

Delaware

Wilmington

DAVIS, C. H.

District of Columbia

Washington

CROWLEY, J. F.
DARNER, H. L.
DAVIS, DANIEL
GARNETT, A. Y. P.
JACOBS, J. B.
KANE, H. F.

McNITT, H. J. RUSSELL

MARTEL, LEON A.

MUNDELL, J. J.

NOTES, BERNARD

PARKER, HOWARD P.

PREECE, ALEC A.

ROSS, J. W.

*SULLIVAN, R. Y.

TITUS, E. W.

WILLSON, PRENTIS

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Jacksonville

STRUMPF, I. J.

Georgia

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BRAWNER, JAMES N., JR.
COLVIN, E. D.
McCORD, J. R.

Augusta

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Savannah

SHARPLEY, H. F., JR.

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BAER, J. L.
BLOOMFIELD, J. H.
BROWNE, W. H.
BUXBAUM, HENRY
CARY, EUGENE
CORNELL, E. L.
CULBERTSON, CAREY
CURTIS, A. H.
DAILY, E. F.
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DeLEE, J. B.
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DORLAND, W. A. N.
EDWARDS, E. A.
FALLS, F. H.
FIELD, MARSHALL
FISCHMANN, E. W.
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FRANKENTHAL, L. E.
FRANKENTHAL, L. E., JR.
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GEIGER, CLYDE J.
GOLDSTINE, M. T.
GOUGH, J. A.
GREENHILL, J. P.
HALL, F. E.
HEANEY, N. S.
HESELSTINE, H. C.
HOLMES, R. W.

President

Prof. Dr. A. H. M. J. van Rooy, Director of the University Clinic of Obstetrics and Gynecology.

Secretary

Dr. F. C. van Tongeren, Deputy Director of the University Clinic of Obstetrics and Gynecology.

PRELIMINARY PROGRAM

TOPICS FOR DISCUSSION

I. Eclampsia. II. Thrombosis and Embolism. III. Hormones.

Reporters:

I. Pathogenesis, Treatment, Dr. E. Klasten, Vienna, Dr. H. Vignes, Paris, and Prof. B. Stroganoff, Leningrad

Eclampsia, from a geographical point of view, Prof. K. de Snoo, Utrecht, and Prof. R. Remmelts, Batavia

II. Diagnosis and Symptomatology, Etiology, Prevention and Treatment, Prof. E. Cova, Torino, Prof. D. Dougal, Manchester, Prof. S. E. Wichmann, Helsinki

III. Historical review, Prof. G. Wagner, Berlin, and Prof. C. Kaufmann, Berlin
Lecture on latest research, Dr. C. Hartman, Baltimore, and Prof. L. Brouha, Liège

Discussors: Dr. M. Cheval, Brussels. Prof. C. Cotte, Lyon. Prof. F. Daels, Gent. Prof. J. Engelhard, Groningen. Prof. L. Fraenkel, Sao Paulo. Prof. J. Frigyesi, Budapest. Prof. P. Gaifami, Roma. Prof. G. Gheorghiu, Bucuresti. Dr. J. Greenhill, Chicago. Prof. H. Guggisberg, Bern. Prof. E. Hauch, Copenhagen. Prof. P. van der Hoeven, Leiden. Prof. Dame A. L. McIlroy, London. Prof. M. Jayle, Paris. Dr. J. Jensen, St. Louis. Prof. H. Kahr, Vienna. Dr. A. Laffont, Alger. Prof. E. Laqueur, Amsterdam. Dr. J. DeLee, Chicago. Prof. W. Liepmann, Istanbul. Prof. N. Louros, Athen. Dr. A. Manevitch, Moscou. Prof. H. Martius, Göttingen. Prof. A. Mayer, Tübingen. Prof. M. Phillips, Sheffield. Prof. R. Schröder, Leipzig. Prof. B. Solomons, Dublin. Dr. F. Taussig, St. Louis. Prof. A. Westman, Lund. Prof. B. Zondek, Jerusalem.

Visitors are advised to apply to the Travel agencies Wagons-Lits/Cook, for reduced fares and for reserving hotel accommodation. Rooms (breakfast, tips and taxes included) can be obtained at prices ranging from D.Fl.3.50 to D.Fl.6.25.

Meetings Will Be Held at the Koloniaal Instituut

Evenings are fixed for receptions, a visit to the Castle "Nijenrode" and Closing Banquet.

On May 8 and 9 there are various trips on the program, including the Reclaiming Works of the "Zuiderzee." A concert, at the "Concertgebouw," by the famous conductor Willem Mengelberg (eighth Symphony of Mahler) has also been arranged. There is also a special program for ladies.

Prospective visitors may become members of the Congress by subscription at the following rates: full members, 15 Dutch florins, associate members (including family), per person, 5 florins. Address the Treasurer, Dr. I. J. Wijsenbeek, "Postgiro rekening, 294741, Amsterdam, Holland.

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SCHUTZ, RICHARD B.
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Springfield
JAMES, J. D.
St. Louis
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CROSSEN, H. S.
CROSSEN, R. J.
DORSETT, E. L.
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entirely normal to those in which uterine bleeding was continuous over a considerable period of time.

We construe as normal those women whose menstrual periods are regular at twenty-eight-day intervals, or close to this, who flow from four to six days moderately, and whose periods are painless. In addition, we have limited our concepts of normal to those women who have had one or more children, in whom pregnancy occurred without undue lapse of time. In the final analysis, the ability to conceive and bear children is our only incontrovertible proof of sexual normality. The abnormal cases represent the usual range of menstrual abnormalities which bring these patients to the gynecologist. All the cases studied were the private patients of one of us (L. W. M.) so that accurate histories and adequate examinations and follow-up were possible.

With few exceptions, all the endometrium specimens were obtained in the office. In these, no anesthetic, local, or otherwise, was used. Specimens were obtained with a very small sharp curette which could in most instances be introduced through the cervix without dilatation. Occasionally, in nulliparas or virgins, slight dilatation of the cervical canal with the smallest Jolly dilator was necessary. We prefer a curette for this purpose to a punch of any sort, since many times we noted the interesting fact that the glandular changes differed considerably in various parts of the endometrium.

The curette is introduced gently through the cervix, carried to the fundus and brought down to the cervix in the positions of 12, 3, 6, and 9 o'clock. Comprehensive samples of endometrium are thus obtained. Sometimes the specimen is obtained by bringing the curette down in a spiral motion from the fundus to the cervix. With proper gentleness, the complaint of cramping pain is minimal, and no patient ever refused further specimens when requested. In no instance was there the slightest deleterious effect, either during the procedure or after.

As stated previously, for several years specimens were obtained at least three times a month, viz., immediately after a menstrual period, at midinterval, and immediately preceding menstruation. However, it was finally definitely concluded that as much could be learned from one specimen, obtained immediately before a menstrual period, as from three or more, and for the past several years, all specimens have been obtained at this time. When uterine bleeding is continuous, it probably makes no difference when they are obtained. From an immediate premenstrual specimen, a complete history of the hormone action on the endometrium since the preceding menstruation can be read, and other specimens obtained during that time are superfluous.

In the interpretation of the accompanying photomicrographs, it is in order to review briefly the present working theories concerning the physiology of menstruation.

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Original Communications

A CORRELATION OF ENDOMETRIAL HISTOLOGY WITH CLINICAL SYMPTOMS*

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IN 1931 we began a study which had for its object the possible correlation of endometrial histology at varying times during the menstrual cycle with estrin concentration, as determined by its extraction from the urine. Daily twenty-four-hour urine specimens were extracted for estrin through one, two, or more menstrual cycles. For several years endometrium specimens were obtained immediately following a menstrual period, at the midinterval, and immediately before menstruation on each patient studied. In a number of cases, specimens were obtained weekly.

It was finally concluded that, as the study was being conducted, no such correlation as was originally thought possible could be shown, and as for obvious reasons daily endometrium specimens could not be obtained over long periods of time, the original purpose of the study was abandoned. Instead, the estrin study was continued separately, and has been reported in another paper. As increasing numbers of endometriums were examined microscopically, a definite correlation of endometrial histology with the clinical aspects of various menstrual phenomena became more and more apparent.

Endometrium specimens have been obtained from over 50 cases, comprising practically the entire range of menstrual phenomena from those

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A normal female sex cycle, therefore, is predicated upon the normal activity of these two ovarian hormones, estrin and progesterone. They must be elaborated in adequate amounts, and there must be a normal balance between them. In the light of our present knowledge, this is

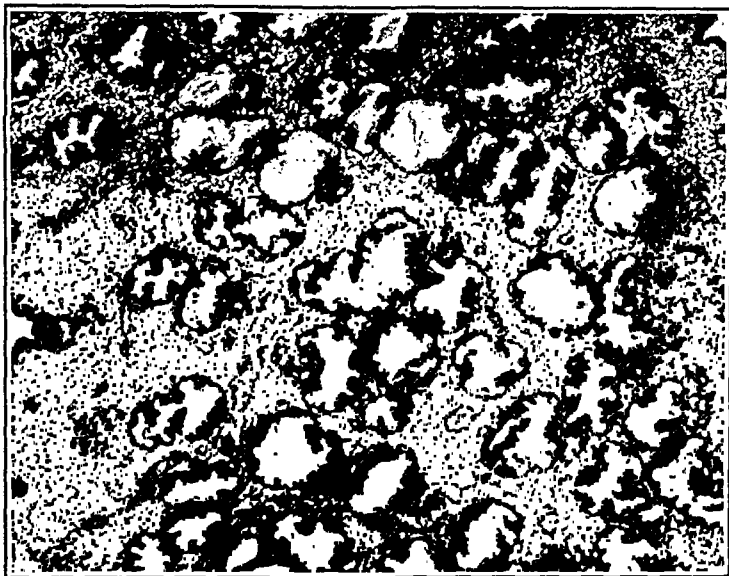


Fig. 2.—K. B., aged forty years. Entirely normal menstrual history. Never any dysmenorrhea. Three normal pregnancies, the last three years ago.



Fig. 3.—D. B., aged twenty years. Entirely normal menstrual history. Never any dysmenorrhea. Now normally pregnant at five months.

in turn dependent upon the proper functioning of the sex hormone or hormones of the anterior hypophysis, which act, although possibly not entirely, through the ovary. While not yet proved, it makes the matter somewhat easier to understand if we follow the postulation of two hypophyseal sex hormones, the follicle stimulating hormone and the luteinizing hormone. The first of these stimulates the development of the

During menstruation, most of the endometrium is desquamated, and immediately following, it is represented in sections by a stroma in which can be seen rather widely spaced uterine glands. These are small and compact, and are lined by a single layer of low cuboidal cells. During the period of follicle growth, the endometrium proliferates. This is marked by a greatly increased vascularity and thickness of the endometrium, and a hypertrophy and hyperplasia of the uterine glands, the cells becoming columnar in type. Following ovulation, which occurs sometime around midinterval, the corpus luteum develops. The hyperplasia of the glands continues, and in addition, becoming noticeable several days before menstruation begins, the glands take on distinct secretory characteristics, which are evidenced in the histologic appearance of the glands by vacuolization of the gland cells, with a charac-



Fig. 1.—M., aged thirty-one years. Entirely normal menstrual history. No dysmenorrhea. Now normally pregnant at eight months.

teristic “fuzziness” of the gland borders. At this time, the lumina are more or less filled with a mucoid material.

The characteristic hormone of the follicle is estrin, and it is under its influence that the glandular hyperplasia occurs, while the characteristic hormone of the corpus luteum is progesterone, which is responsible for the secretory changes which occur premenstrually in the glands. However, estrin is secreted by the corpus luteum also, in even greater amounts than by the follicle. The function of progesterone seems to be to prepare the endometrium for the nidation of the fertilized ovum. Its full and complete action also seems to be necessary for normal menstruation, i.e., for menstrual periods which begin and end sharply, which last for a normal length of time with moderate flow, and which are free from pain. We have not found a premenstrual endometrium which we considered normal in any patient whose menstrual periods did not fulfill these requirements.

follicle with its elaboration of estrin, and both, but particularly the latter, are responsible for the development of the corpus luteum and its particular hormone progesterone.

Figs. 1, 2, and 3 are photomicrographs which represent what we consider normal endometriums. There is a normal hyperplasia of the



Fig. 6.—B., aged twenty-four years. This patient's periods were regular, but the duration was from eight to twelve days. Flow was quite excessive. Patient was in a sanitarium in Denver with an active tuberculosis. That the tuberculosis was probably not a factor in the menstrual abnormality, note the following section: This section shows a normal, or even an increased, glandular hyperplasia, but the progesterone influence is slight, reflected in almost absent secretory characteristics in the glands.



Fig. 7.—F. M., aged thirty-three years. Symptoms in this case were almost identical with those of the preceding one, i.e., regular menstrual intervals, but flow was prolonged and quite excessive. There have been times when the hemoglobin has fallen from 90 per cent to 55 per cent during a single menstruation. Patient is married and has two children, the youngest five years of age. Since that time there has been a spontaneous abortion at two and one-half months.

As noted, this patient's symptoms are practically identical with those of the preceding patient, and their endometriums are practically identical.

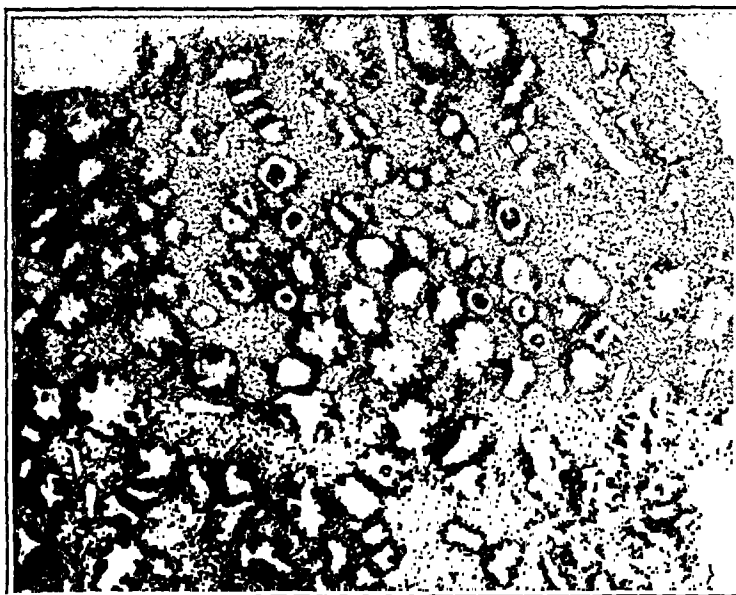


Fig. 4.—G. O., aged twenty-one years. History of previous pelvic infection, probably gonorrheal. Alternating menstrual periods of four and nine days' duration. Intervals normal. Flow not excessive in either case. Specimen taken just before an expected nine-day menstruation. Decreased secretory activity of the glands is apparent. Operation was done, at which time both tubes (abscessed) and right ovary, which was imbedded in scar tissue and polycystic, were removed. Following this, periods were all of four days' duration, painless and with moderate flow. Evidently the alternating nine-day periods were controlled by the diseased right ovary. Unfortunately, it was impossible to obtain a subsequent endometrium specimen. We believe it would have been normal.



Fig. 5.—I. M., aged twenty-six years. Normal menstrual history. One normal pregnancy shortly after marriage. No pregnancies for five years. Then followed 2 spontaneous abortions at an interval of a year. Next pregnancy continued after a threatened abortion at two months. From this time until term, patient was treated continuously with pregnancy urine extracts. Baby normal. One and one-half years later there was another pregnancy. No treatment was given during this pregnancy, which ended in a miscarriage at six months.

This endometrium shows considerable diminution of progesterone influence, reflected in a decreased secretory activity of the glands. Menstruation and/or fertility are probably never normal in an individual who shows this much hormonal imbalance.

women. With the exception of the endometriums of this type, all were obtained from women in the optimum child bearing age.

The gradation of clinical symptoms corresponding to the endometrial specimens may be listed as follows:

1. Normal. Menstrual periods regular at intervals of approximately twenty-eight days; duration of flow four to six days, in moderate amount; beginning and end of flow sharply delimited; no dysmenorrhea (Figs. 1, 2, 3).



Fig. 8A.

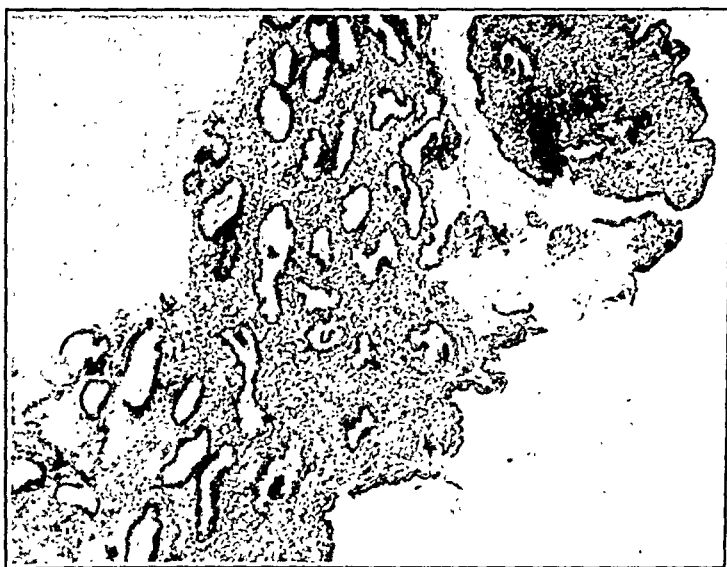


Fig. 8B.

Fig. 8.—E. S., aged twenty-one years. These three specimens (*A*, *B*, and *C*) were obtained immediately preceding menstruation in three successive months. There was one normal pregnancy, which occurred shortly after marriage. Since that time extensive pelvic surgery has been done for salpingitis and adhesions. Both ovaries remain. Patient complained of gradually decreasing menstrual intervals with lengthening duration of flow. Flow rather scanty and "splotchy" in type.

It is interesting how alike these three specimens are. The glands are not normally hyperplastic. Secretory characteristics are slight. It is evident that not only is the progesterone influence defective, but that of estrin is also.

glands, and they show well the normal premenstrual secretory characteristics, as evidenced by the "fuzzy" appearance of their inner borders. An endometrium of this type presupposes a normal follicle development with rupture and the development of a normal corpus luteum. It also presupposes the extrusion of a normal ovum when the follicle ruptures, but this may not necessarily be so, nor has it been proved as yet. From the hormone standpoint, an endometrium of this kind can only result when there has been a normal elaboration of estrin by the follicle, and of estrin and progesterone by the corpus luteum, and of a normal balance of activity between them.

At the other end of the series we find the familiar and typical "Swiss cheese" pattern of endometrium, which is believed to result from a long continued excessive action of estrin, and an absence of that of progesterone. In this type of endometrium, the hormone balance is completely destroyed. In conjunction with such endometria, one finds ovaries which are polycystic, resulting from derangements in follicle maturity and rupture, and in which signs of current corpus luteum activity are absent. This is the type of nongravid endometrium with which the pathologist is most familiar for the reason that curettages are not usually done in the great number of patients whose menstrual abnormalities are of lesser extent than the continuous bleeding which nearly always results from such endometria. We have not found such endometria except in women in or at the menopause, and it is in these that a curettage is of paramount importance for diagnostic purposes.

We present a series of endometria which fall in between the normals at the one end and the "Swiss cheese" type at the other, in which the departure from normal of each shades into an increasing departure from normal of the next. The patients' menstrual symptomology shows a similar gradation in severity, which can be correlated with the endometrial picture. It was of the greatest interest to us in examining a new specimen to observe how similar it always was to a former one from a patient with similar menstrual complaints and symptoms. The photomicrographs which follow are arranged in this series, and the salient points in the history of each case are presented.

It is evident that these endometria grade almost imperceptibly into each other in the extent of pathology or hormone imbalance involved. The most characteristic feature in each succeeding specimen is the evident gradually diminishing progesterone action on the endometrium. There may or may not be evidence of excessive or diminished estrin action. We have not found any endometrium in which we could interpret anything pointing to excessive progesterone influence. It is of interest that no endometria such as those shown in Figs. 11, 12, and 13 were found except in women in or at the menopause. None which showed so marked a departure from normal were found in younger

6. Menstrual rhythm entirely lost and bleeding usually continuous (Figs. 11, 12, and 13).

It appears then, that menstrual abnormalities can be closely correlated with the histology of the endometrium, and that variations from normal here are due to an imbalance between the two ovarian hormones, estrin



Fig. 10.—B. F., aged twenty-two years. For the first time in this series, we have the endometrium of a patient who occasionally flows from one menstrual period into the next. She is markedly overweight, and shows unmistakable evidence of pituitary deficiency. The section is the first which does not show in a single gland any evidence of progesterone activity. This specimen was taken about one hour after menstruation had begun. Estrin influence is greatly diminished also. Pelvis is grossly negative.

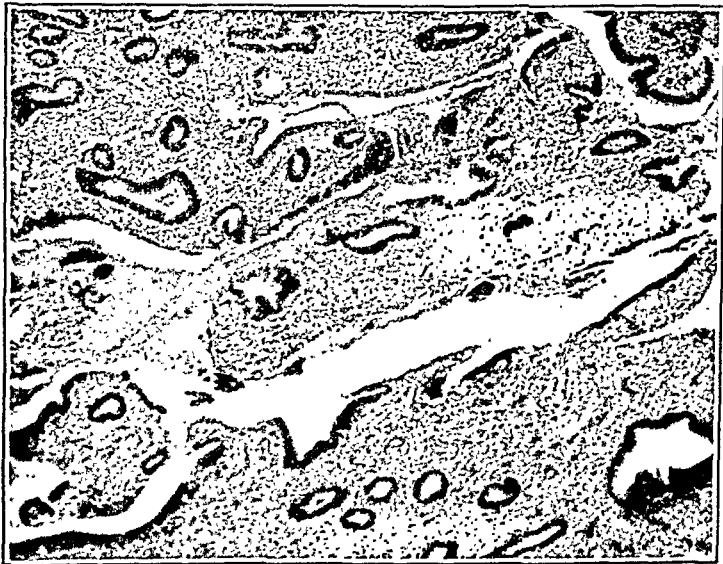


Fig. 11.—G. F., aged forty-three years. Specimen from a patient who had flowed continuously for two months. Menstrual periods were essentially normal until several months before, when they became irregular with increasing duration of flow. Endometrium was markedly thickened. This final marked departure from normal in the patient's symptoms was of relatively recent origin, and although the hyperplasia was marked, the glandular pattern shows only beginning cystic degeneration of the glands. No evidence whatever of corpus luteum activity.

2. Normal intervals, but duration of flow is lengthened, and frequently amount is excessive. Flow may "dribble out" for several days at the end (Figs. 4, 6, 7).

3. Intervals still fairly regular, but duration of flow is considerably lengthened, sometimes for two weeks. Flow may vary from scanty to profuse several times during this period (Fig. 8).

4. Intervals irregular, with varying duration and amount of flow (Fig. 9).

5. Intervals usually irregular, and duration of flow lengthened so that one period almost lasts into the next one, but always some interval, of varying length, in which there is no bleeding (Fig. 10).



Fig. 8C.



Fig. 9.—W. R., aged thirty-one years. This woman has had several pelvic operations. Her original complaint was dysmenorrhea. She still has considerable pain at times. There was one child, and pregnancy occurred shortly after marriage. For the past three years, periods have lasted for two weeks many times, and there is varying scanty flow and flooding in the same period. The right ovary has been removed because of "cysts." Pelvic examination is at present essentially negative, except that the remaining left ovary is quite small and hard. Both estrin and progesterone deficiency are more marked in this section than in the preceding one. The glands show less hyperplasia and less premenstrual changes. The stroma is thin and edematous.

glands is necessary to produce a premenstrual endometrium which we have described as normal.

As a result of our experience over a period of six years, we are of the opinion that the curettage of the nongravid uterus, of sufficient thoroughness to secure ample tissue for purposes of microscopic study, is a minor office procedure, and can be done with relative impunity. No anesthetic is necessary.

Without appending in detail the voluminous bibliography which would be necessary, we desire to acknowledge all of those workers in this and related fields who have contributed to our present knowledge of the physiology of the female sex cycle.

HEMORRHAGIC DISEASE OF THE NEWBORN

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(From the Department of Obstetrics and Gynecology, Cornell University Medical College and the New York Hospital)

THERE is a tendency in the newborn infant to bleed spontaneously from the mucous membranes during the first days of life. This condition has been termed: "idiopathic hemorrhage," "hemorrhagic diathesis," "hemophilia neonatorum," "umbilical hemorrhage," "melena neonatorum," "hemorrhagica neonatorum," and "hemorrhagic disease." The etiology remains obscure.

Hemorrhagic disease is either present at birth or occurs soon thereafter. The mortality is high unless human blood is promptly administered. Consequently, the accoucheur is responsible for its recognition and treatment. Stander has advocated that the total infantile mortality rate should include all deaths, regardless of cause, occurring in the first fourteen days of life. Therefore, a successful confinement entails the delivery of a "good baby," and one that remains so for fourteen days. For these reasons, the present study of hemorrhagic disease of the newborn was made, placing emphasis on obstetric and parturitional factors that appear to be contributory.

HISTORICAL REVIEW

Omphalorrhagia was first described by Watts in 1753. Rilliet in 1848 commented on intestinal hemorrhage in newborn infants. In 1850, Bowditch pointed out the association of such bloody dejection with umbilical hemorrhage. He considered this syndrome to be very rare, since it was not mentioned in the leading medical texts and journals of that period. This caused Minot in 1852 to state that "during the past few years, numerous instances have been reported." Minot reiterated the contention of Bowditch that umbilical bleeding was a manifestation of a diathesis, with co-existing bleeding from the gums, stomach, and intestine.

Coale in 1852 described hemorrhagic disease as it is known today. He reported a case that bled from the stomach and anus, without umbilical bleeding. This report

and progesterone. The cause, in turn, of this imbalance may not lie in ovarian pathology per se, but may be due to abnormalities in the anterior lobe of the hypophysis, or even to pathology in other endocrine glands. In fact, we believe, so far as the female sex cycle is concerned, that a normal activity of, and balance between, all of the endocrine

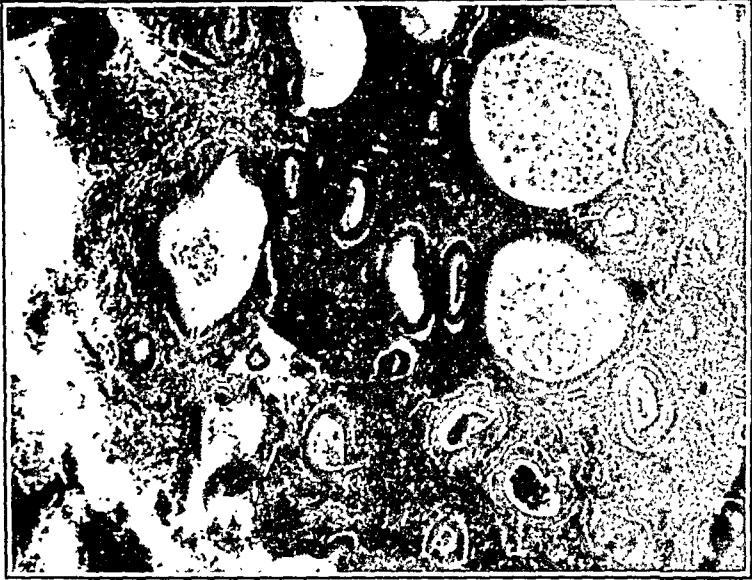


Fig. 12.—E. G., aged forty years. The hormonal imbalance is still farther along in this case. In 1932, after a period of amenorrhea of three months' duration, during which time the patient thought herself pregnant, she began to flow excessively, and continued to do so until curettage was done three weeks later. Eighteen months later the same history repeated itself, and again twelve months later. The specimen shown was obtained after the second period of menorrhagia. The endometrium was so hyperplastic that it resembled pieces of placental tissue. Differing from the preceding specimen, in which only an occasional gland is dilated, in this one most of them are, and a considerable number are definitely cystic.

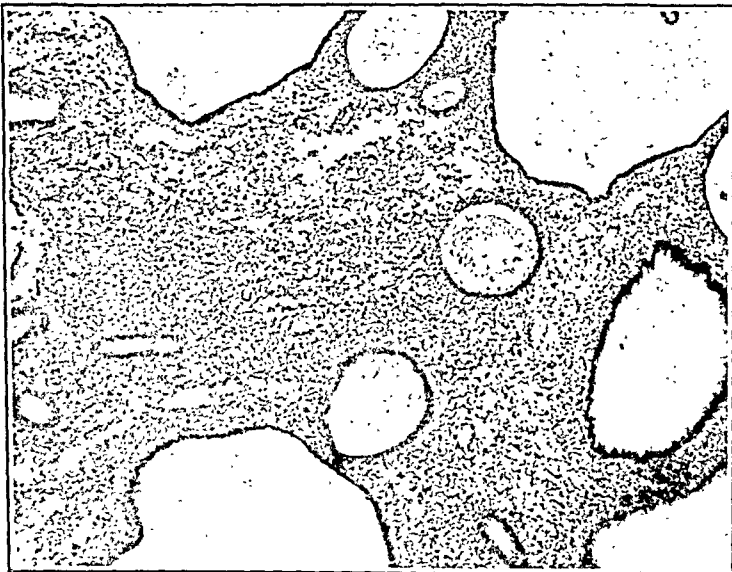


Fig. 13.—B., aged forty-one years. This patient has had menorrhagia for the past three years, and had been flowing continuously for the last seven months. Section shows enormous dilatation and cystic degeneration of the glands. This section represents the end histologic picture found in this type of case, i.e., constant uterine bleeding over long periods of time. It is the typical "Swiss cheese" pattern of endometrium.

Parity.—Primiparas contributed 35 or 48.6 per cent of the cases, with 52.2 per cent for the control. Multiparity was present in 37 or 51.4 per cent of the cases, with 48.7 per cent for the control. Multiparity is slightly increased, but is believed to have little direct significance.

Complications of Pregnancy.—Antepartum complications occurred in 45 or 62.5 per cent of the mothers, as compared with 22.3 per cent in the control. This difference of nearly 300 per cent is shown in Table I. The toxemias were grouped according to the classification in Stander's monograph. Sahli hemoglobin determina-

TABLE I. THE FREQUENCY OF ANTEPARTUM COMPLICATIONS OF PREGNANCY

		CASES	PER CENT	CONTROL
Anemia	(44 patients)	16	36.3	4.0
Toxemia	(72 patients)	14	19.5	10.8
Syphilis	(72 patients)	6	8.3	3.0
Other	(72 patients)	9	12.5	4.5
		45	62.5	22.3

tions in the last trimester of pregnancy averaged 65 per cent in 44 cases studied, of which 16 cases were below 70 per cent. Cardiac disease, pyelitis, and pulmonary tuberculosis constitute the group marked "other." The high incidence of the complications of pregnancy, together with the increased age and racial factors, make maternal debility a decided entity.

Pelvis.—Abnormal pelves were present in 10 or 13.8 per cent of the cases, which is higher than the control of 8.4 per cent. Therefore longer labors and more operative deliveries may be expected.

Duration of Labor.—The duration in primiparas was 24.3 hours, and 12.5 hours for the multiparas, in the hospital cases; while on the outdoor service, all cases being in multiparas with an average of 10.6 hours. The usual duration in primiparas is eighteen hours, and about twelve hours for multiparas. The prolonged labor in primiparas is significant since nearly half of the cases of hemorrhagic disease occurred in first-born infants. Labor exceeded twenty-four hours in 15 cases, with an average duration in these of forty-one hours. Unfortunately, information regarding the frequency and intensity of the uterine contractions was not available.

Operative Incidence.—Operative delivery including breech extraction, was performed in 16 or 22.2 per cent of the cases, the control being 15.7 per cent. They were: midforceps, 7; low forceps, 5; breech extraction, 2; cesarean section, 1; version, 1. The indications were: fetal distress, 3; prolonged second stage, 5; maternal exhaustion, 2; prolapsed cord, 1; persistent occiput posterior, 2.

Premature Rupture of the Membranes.—This occurred in 18 or 25.0 per cent of the cases, which coincides with the control of 25.8 per cent. "Dry labor" was apparently not a factor.

Medical Induction and Rectal Analgesia.—This form of quinine medication was administered to 39 or 62.9 per cent of the mothers delivered in the hospital, and is over 200 per cent more than the control, as shown in Table II. Perhaps longer labors increased the need for analgesia. The dosage of quinine given orally was 0.6 gm., usually followed by 0.3 gm. in one hour. The dosage of quinine given rectally was 1.3 gm. in 7 cases; and 0.6 gm. in 17 cases, the latter dosage was repeated in 5 cases. The average time interval between medication and delivery was 30.1 hours for the oral, and 10.8 hours for the rectal administration. No definite conclusions can be drawn regarding quinine as an etiologic factor, although quinine hemolysis has been reviewed by Terplan and Javert in early pregnancy.

Other Drugs.—Bismuth and arsphenamine were given to 5 mothers. The average dosage of bismuth was 0.1 to 0.3 gm.; arsphenamine 1.5 to 3.7 gm. Morphine and

remained unnoticed, for later in 1885, Thayer reported 5 cases of umbilical bleeding occurring in 24,533 infants, and commented on the associated hemorrhage from the stomach and bowels.

Townsend in 1894 clarified the situation by stating that it was a common error to think of hemorrhage only in relation to the umbilicus. He reported 50 cases in a series of 10,700 infants that had multiple hemorrhagic lesions. Umbilical bleeding was present in 18 cases. Townsend named this syndrome "hemorrhagic disease of the newborn."

During the past forty years other advances have been made. These will be mentioned in the discussion, together with etiologic references. The reader is referred to the publication of Von Reuss, and of Schloss and Commiskey, for additional etiologic information.

THE PRESENT STUDY

This study has been conducted from the records of 11,303 mothers and their infants. The cases comprise the full-term and premature deliveries on the public indoor and outdoor services of the Woman's Clinic, covering the period from September, 1932 to April, 1936, inclusive. Of 8,019 infants born in the hospital, 62 developed hemorrhagic disease, while on the outdoor service (Berwind Free Maternity Clinic) only 10 cases occurred in 3,284 infants delivered, making a total of 72 cases. All but 5 of these infants were cared for by the Pediatric Service of the New York Hospital.

Control statistics are from two sources, unless otherwise stated:

1. The Annual Report of the New York Lying-In Hospital for 1935 based on 3,488 full term and premature deliveries.
2. A series of 1,870 consecutive deliveries in this clinic now being studied for another purpose by Pastore.

The author is aware of the fallacy of comparing a small group of cases with large control series. Nevertheless, the deductions obtained are of value as clues, to be confirmed or refuted by further observations. Follow-up studies on the infants beyond the neonatal period of fourteen days are not within the scope of this paper.

MATERNAL STATISTICS

The records of the 72 mothers whose infants developed hemorrhagic disease were reviewed as follows:

Age.—The average maternal age was 30.0 years, which is above the age reported by Peckham and Kuder of 23.8 years. The primiparas averaged 25.7 years, and the multiparas 34.0 years. This forecasts prolonged labor, and an increased tendency towards obstetric abnormalities.

Race.—There were 16 cases or 22.2 per cent in the black race, while the clinic registration is only 12.2 per cent. This indicates a tendency in a race of established debility. One Chinese infant developed the disease. Further racial differentiation was not conclusive.

Drugs Used Postpartum.—Pituitrin and ergot preparations were both given to practically all of the patients. No definite conclusions can be made, since the transmission of these drugs to the infant through the colostrum in sufficient amounts has not been established.

INFANT STATISTICS

The records of the 72 infants born to the mothers presented above were analyzed as follows:

Incidence.—Of the 8,019 infants born in the hospital, 62 developed hemorrhagic disease, giving an incidence of 0.773 per cent. On the outdoor service, 10 of the 3,284 infants developed the disease, or 0.304 per cent. A comparison with Townsend's figures is given in Table V. That the incidence is over 100 per cent greater in the hospital-born babies deserves investigation. The lower incidence on the outdoor service was not due to failure in recognizing the cases, since the same obstetric staff supervised both services.

TABLE V. THE INCIDENCE OF HEMORRHAGIC DISEASE

	INDOOR SERVICE				OUTDOOR SERVICE		
	NO. OF CASES	YEAR	CASES	IN- CIDENCE	NO. OF CASES	CASES	IN- CIDENCE
New York Hospital	8,019	1936	62	0.773%	3,284	10	0.304%
Boston Lying-In	6,700	1894	46	0.67	4,000	4	0.10

Heredity.—Nothing definite can be said. Only 4 of the mothers returned for subsequent delivery and all had normal infants. Minot and Kugelmass have pointed out the occurrence in successive pregnancies.

Sex.—Males were affected in 49 or 68.0 per cent of the cases. Townsend, Capon, and Dembo found the sexes about equal.

Birth Weight.—The average weight was 3380 gm. (7.5 pounds), the control weight being 3,427 gm.

Duration of Gestation.—Using the duration of 280 days as normal, the average duration of pregnancy was 275 days; 40 infants, or 55.5 per cent, had a duration of 264 days, and these averaged 3,048 gm. in weight. This indicates a definite tendency toward immaturity, which was also shown by the increased incidence of premature infants.

Prematurity.—Seven or 9.7 per cent of the infants weighed less than 2,500 gm., while the clinic incidence of prematurity is only 2.0 per cent. This shows a decided preponderance of premature infants. All infants weighing less than 2,500 gm. and under 45 cm. in length are considered prematures. Babies weighing less than 1,500 gm. were excluded.

Weight Loss.—The average initial loss was 257 gm. which agrees with the figure of 250 gm. given by Williams.

Infant Feeding.—This was routine and did not appear to be a factor.

Pyrexia.—Temperature above 37° C. was present in 14 or 19.4 per cent of the cases; of these 5 had bronchopneumonia. Townsend found fever in nearly all of his cases. Tyson found fever in 14 per cent of newborn infants, the chief causes being inanition and dehydration.

Rash.—Dermatitis was present in 23 cases. The routine use of ammoniated mercury reduces the value of this observation. However, a drug eruption (quinine, ergot) may have produced some of these reactions.

Jaundice.—This was present in 15 or 20.8 per cent of the cases and is in agreement with the figure of 20 per cent quoted from DeLee.

TABLE II. THE USE OF QUININE IN 62 HOSPITAL CASES

	CASES	PER CENT	CONTROL
Medical induction	15	24.2	4.7
Rectal ether	24	38.7	22.2
	39	62.9	26.9

scopolamine, nembutal, codeine, aspirin, pyramidon, were used in a small number of cases. Ten mothers received iron therapy.

Anesthesia.—The effect of anesthesia has been tabulated in Table III. No anesthesia, nitrous oxide alone, and ether alone, seemed to produce more cases. When ether was added to the nitrous oxide, fewer cases occurred. This may be due to the addition of oxygen along with the ether, and supports the anoxemia theory as advocated by Graham.

TABLE III. THE EFFECTS OF ANESTHESIA

	CASES	PER CENT	CONTROL
No anesthesia	14	19.4	4.7
Nitrous oxide	19	26.3	16.0
Ether alone	6	8.3	3.4
Nitrous oxide, oxygen, ether	33	45.8	75.5
	72		

Placenta.—The average weight was 667 gm., which is normal. Only 8 or 11.1 per cent of the placentas were abnormal. This is lower than the figure of 18.0 per cent reported by Traut. The abnormalities included: placentitis 3, endarteritis, circumvallation, blood cysts, fibrinoid degeneration, hemochromal degeneration 1 case each. There was suggestive evidence of placental syphilis in only 1 case.

Blood Loss in Third Stage of Labor.—The blood loss in the cases measured by the Pastore apparatus averaged 371 c.c., which was 100 c.c. greater than the control. In this group postpartum hemorrhage (600 c.c. or more) was 265 per cent more frequent. This increase was also noted in the estimated cases, and is shown in Table

TABLE IV. THE BLOOD LOSS IN THE THIRD STAGE

	CASES	AVERAGE LOSS	CONTROL LOSS	POSTPARTUM HEMORRHAGE		
				CASES	PER CENT	CONTROL
Measured	32	371 c.c.	271 c.c.	6	18.8	7.1
Estimated	40	320 c.c.		3	7.5	3.2
	72					

IV. The increased incidence of postpartum hemorrhage was apparently due to the greater frequency of anesthesia, analgesia, operative delivery, prolonged labor, etc., which, according to Pastore, tend to produce excessive blood loss. Perhaps these factors, which cause increased bleeding in the mothers, may also influence the infants to bleed abnormally.

Maternal Morbidity and Mortality.—Temperatures were taken every four hours. Two rises above 38° C., on two successive days not including the first twenty-four hours, constitutes a febrile puerperium. This was present in 16 or 22.2 per cent of the cases, with 10.6 per cent in the control series. This increased morbidity is to be expected, because of the larger number of operative deliveries and the greater incidence of postpartum hemorrhage as well as increased maternal debility. There was one maternal death due to peritonitis.

the first week of life, 7 additional cases of anemia were discovered, making a total of 10 cases out of 41, or 24.3 per cent, with anemia. Whether these were primary or due to the hemorrhagic process is conjectural.

The increased number of nucleated red cells is interpreted as evidence of prematurity although erythroblastosis should be considered. Parsons and Hawksley

TABLE VIII. BLOOD STUDIES ACCORDING TO DAY OF ONSET AND OF LIFE

	RED COUNT	GM. HG	WHITE COUNT	PLATELETS	DIFFERENTIAL COUNT	
					LYMPHS	NORMO-BLASTS
First day	5,200,000 (13)	20.8 (12)	18,100 (11)	162,000 (7)	30	13.0 (10)
Second day	5,200,000 (13)	21.6 (11)	16,000 (11)	154,000 (9)	33	2.5 (12)
Third day	5,200,000 (6)	21.0 (6)	13,800 (7)	290,000 (2)	38	4.0 (6)
Fourth day	4,900,000 (3)	21.6 (3)	9,800 (3)	290,000 (2)	39	0.0 (4)
Fifth day	5,900,000 (3)	22.2 (3)	19,900 (3)	200,000 (2)	17	0.0 (2)
Control Lucas	5,500,000		19,900	305,000	20	1.0

(Figures in parentheses indicate number of cases studied)

state that the premature infant has nucleated red cells in direct proportion to the degree of prematurity. Terplan suggested that these cells can be enumerated in the fetal capillaries on histologic section of the placenta. This has been worked out by Ryerson and Sanes.

Blood Grouping.—All infants receiving transfusions were grouped and cross matched. The distribution of the groups was within the expected limits.

Treatment.—The type of therapy with results is presented in Table IX. The average amount of blood given by transfusion was 60 c.c.; citrated blood was used in all transfusions. The average amount of whole blood given intramuscularly was 18 c.c. A comparison of results with other investigators is given in the same table.

TABLE IX. THE TYPES OF TREATMENT

	CASES	DEATHS	MORTALITY	CASES	MORTALITY	INVESTIGATOR
None	8	4	50.0%	46	84.0%	Minot
				50	62.5	Townsend
Whole blood	16	0	0.0	27	10.7	Capon
Blood serum	0			13	0.0	Welch
Transfusion	14	2	14.2	43	2.3	Robertson
Whole blood and transfusion	36	5	13.8	21	4.7	Wing

Mortality.—There were 11 deaths, giving an uncorrected rate of 15.7 per cent; while the clinic rate is 3.34 per cent. The mortality rate was highest when no human blood therapy was administered. Three infants weighing less than 2,000 gm. each are included. Of the 11 deaths, 10 occurred in the first week of life; 3 of these on the first day of life. During the period covered by this study, the total number of infantile deaths was 439, of which 11 or 2.5 per cent were caused by hemorrhagic disease.

Causes of Death.—Autopsies were performed on 10 of the 11 infants; all but 3 of these were done in the Department of Pathology. The chief pathologic findings comprised:

1. Bronchopneumonia 5 cases, one of which had gastrotomy.
2. Intracranial hemorrhage 3 cases; one was a 1,360 gm. infant with bilateral tentorial lacerations; one had an associated anemia with a hemoglobin of 35%; the last was suspected clinically but no autopsy was obtained.

Syphilis.—The serology, x-ray of long bones, autopsy, or placental sections, did not definitely reveal the presence of congenital syphilis in the infants born to mothers with positive serology, although there was suggestive evidence in 2 cases. However, Mracek found that 14 per cent of 132 cases of congenital syphilis had hemorrhagic lesions.

Resuscitation.—The necessity for the use of the Flagg technique is a fairly accurate index of asphyxia; it was used in 7 or 11.2 per cent of the hospital cases. McGrath and Kuder found that it was used in 3.0 per cent of the infants born in the clinic. The increase may be due to the greater number of premature infants, operative deliveries, longer labors, anesthesia and analgesia. Whatever the causes may be, the fact remains that anoxemia resulted, requiring resuscitation.

Source of Hemorrhage.—The clinical observations are presented in Table VI. Over half of the infants had two or more lesions. The multiplicity indicates the generalized manifestations of the process, which is corroborated by autopsy (see Table X).

TABLE VI. THE SOURCES OF HEMORRHAGE IN THE INFANTS

Emesis	31	Cord	7	Mouth	3
Melena	12	Foreskin	6	Urine	2
Petechiae	7	Vagina	6	Eyes	2

Time of Onset of Bleeding.—More than one-third of the infants developed bleeding within the first day of life, as shown in Table VII. For each succeeding day there is a progressive decline in the number of cases that begin to bleed. For practical purposes, it can be said that bleeding does not occur after the first week of life. Diamond states that bleeding usually occurs between the third and sixth days of life.

TABLE VII. BLEEDING ACCORDING TO DAY OF ONSET

	CASES	PER CENT
First day	25	34.7
Second day	14	19.5
Third day	13	18.1
Fourth day	9	12.5
Fifth day	5	6.9
Sixth day	4	5.5
7th day and over	2	2.8

Bleeding Time.—The Duke method was done in 38 cases, with an average of 14.2 minutes. Rodda states that four minutes is normal. The majority of the cases had normal bleeding times. However 11 were definitely prolonged with an average of 44.2 minutes.

Clotting Time.—The capillary tube method was used in 36 cases, with an average time of 9.7 minutes. Rodda gives seven or eight minutes as the maximum normal range. The majority of the cases were normal, while 10 cases were definitely prolonged with an average of 27.4 minutes. The infants with prolonged bleeding time invariably had a normal clotting time and vice versa. These determinations have a diagnostic value when prolonged, and serve to indicate the cases that are more severe.

Blood Studies.—Complete or partial studies were made in 41 cases, and they are summarized in Table VIII. The examinations were done on the day of onset of bleeding which corresponds to the day of life. There is no marked deviation from the control figures of Lucas for the first day of life. Of 15 infants studied on the first day, 3 had an average red cell count of 2,900,000, which if omitted from the average of the first day would increase the average count to 5,700,000. During

tory apparatus is likewise immature, with incomplete elastic and connective tissue formation. The majority of the infants were more than two weeks from term, while 9.7 per cent were premature infants. Therefore immaturity and prematurity are definite factors in increasing the incidence of hemorrhagic disease.

The relationship to labor is further established by the fact that over one-third of the cases developed bleeding within the first twenty-four hours of life, while the rest showed signs of bleeding soon thereafter. Petechiae and hemorrhages should be looked for at the time of delivery. Often trauma to the ankles caused by holding the infant at this point, may produce the first petechiae to be visible. Clinically, and in the order of frequency, blood-tinged emesis, melena, skin petechiae, bleeding from the cord, were noted. At autopsy ecchymoses and petechiae were found in the internal organs in varying degree of severity. Every pathologist acquainted with autopsies on the newborn, has seen such hemorrhages even after a normal labor. However, since 34 per cent of the infants showed clinical bleeding on the first day of life, and since 3 infants died on the first day of life of hemorrhagic disease, and because hemorrhagic lesions are often encountered in infants at autopsy; it is more than probable that hemorrhagic disease runs part of its course intra-utero. The frequency of the pathologic lesions further suggests that many infants recover spontaneously, while others die with or without clinical evidence of bleeding. In the present series 4 cases, or 5.5 per cent, recovered without the benefit of therapy.

Intracranial hemorrhage has been found associated with these ecchymoses, and Green first pointed out that intracranial hemorrhage may be due to "dyscrasia hemorrhagica neonatorum." In 36 routine autopsies on newborn infants, Warwick found brain hemorrhages in 18; of these 8 had hemorrhagic disease. Dembo also noted 15 cases of intracranial hemorrhage in 55 cases of hemorrhagic disease. In our series, subarachnoidal, subdural, ventricular, and cerebral hemorrhages were present in 6 of the 10 cases at autopsy. Foote has stated that hemorrhagic disease may first manifest itself as intracranial hemorrhage.

Judging from the reports in the literature since 1850, when Bowditch pointed out the rareness of hemorrhagic disease, and West's failure to find a single case in 16,276 infants, this syndrome appears to be on the increase. Furthermore, the increase is more pronounced in hospital-born infants, with an incidence of 0.773 per cent as compared with 0.304 per cent on the outdoor service. The difference is partly due to the fact that all abnormal maternal cases were hospitalized. The outdoor service cases did not receive anesthesia, medical inductions or analgesia containing quinine. There were no primiparous mothers in the outdoor group, nor were any of the infants premature. The incidence on the outdoor service is greater than Townsend's figure of 0.10 per cent. This is attributed to the fact that 50 per cent of the outdoor cases were in the

3. Aspiration of amniotic fluid, 2 cases.

4. Not known, one case.

Associated Pathology.—The internal organs had multiple hemorrhagic lesions as shown in Table X. Many organs were also congested and hyperemic. If these lesions are correlated with the clinical evidence of bleeding, then hemorrhagic disease is a generalized systemic process. No gastric or intestinal ulcers were present. There was no evidence of syphilis. Congenital anomalies were found in 2 cases: atresia of the common bile duct and tracheo-esophageal fistula. Jaundice and anemia were noted in 2 cases each. Atelectasis was found in 4 cases. There was bloody fluid in the pericardial cavity in 4 cases, the pleural cavity in 2 cases, the peritoneal cavity in 1 case. Erythropoiesis was noted in the liver in 2 cases, in the spleen in 1 case. Blood cultures were not conclusive.

TABLE X. HEMORRHAGIC LESIONS IN THE INTERNAL ORGANS AT AUTOPSY

LESION	ORGAN	CASES	ORGAN	CASES
Ecchymoses and Hemorrhages	Pericardium	4	Liver	1
	Pleura	3	Intestine	2
	Thyroid	2	Mesentery	1
	Thymus	3	Bladder	1
	Adrenal	2	Testicle	2
	Kidney	2	Mediastinum	1
	Tentorium	2	Subarachnoid	1
	Brain	1	Subdural	1
Hyperemia and Congestion	Lungs	3	Intestine	2
	Thyroid	2	Kidney	2
	Liver	3	Pancreas	1
	Spleen	4	Heart	1

DISCUSSION

This study has disclosed evidence indicating that hemorrhagic disease of the newborn is influenced by antenatal and intranatal factors. Previous authors have minimized the maternal aspects, i.e., Townsend and Capon, although Wing mentioned long hard labors as a predisposing factor.

The mothers in this series experienced abnormal pregnancies and labors. They were exposed to this by being older than the average child-bearing woman. Labor was often long, hard, and difficult, as indicated by the prolongation of labor, the increased incidence of operative deliveries, and premature separation of the placenta in 2 cases. Abnormal pelvises were also more prevalent. Information regarding the frequency and intensity of the uterine contractions was not available.

How does labor influence hemorrhagic disease? Physiologically, each uterine contraction forces blood from the placenta into the fetal circulation, raising the arterial and venous tension simultaneously. The elasticity of the vessels and capillaries permits considerable dilatation and distension. The resulting engorgement and congestion is a matter of degree. Should the forces of labor be unusually severe, then the separation of the capillary endothelial cells, or actual rhexis of the vessels, is to be expected. Blood then oozes into the tissues. This endothelial asthenia is more pronounced in immature infants whose circula-

Dietary restrictions during the antenatal period and during parturition may precipitate a derangement in the prothrombin-antithrombin equilibrium, thereby affecting the coagulability not only of the mother's blood but also that of the infant. The treatment of toxemia of pregnancy by a low protein diet illustrates this view. Kugelmass raised the prothrombin values in the mother with a proper diet, and thereby was able to prevent hemorrhagic disease. Certainly the role of prothrombin merits investigation. Perhaps it is also a factor in postpartum hemorrhage. Moore and Brodie have reported a deficiency of vitamin B as a factor.

Whipple states that prothrombin and antithrombin are in delicate equilibrium, and that when antithrombin is in excess, purpura and bleeding are to be expected. In this series the average bleeding time was prolonged, and the clotting time was slightly above normal. One can conclude that abnormal clotting factors do not produce hemorrhages *per se*, but rather allow bleeding precipitated by the forces of labor to continue.

Howell's theory requires five factors. In hemorrhagic disease these are present as follows:

Platelets	present, (Table V)
Calcium	normal (Lucas)
Prothrombin	low (Whipple, Lucas, Kugelmass)
Antithrombin	excessive (Howell, Kugelmass)
Fibrinogen	normal (Whipple)

The derangement appears to be in the prothrombin-antithrombin balance. No studies were made to correlate this with the other clotting factors. However, an understanding of Howell's theory is essential, since it provides a clue which appears to be of value in the treatment of hemorrhagic disease. Whole blood or transfusion evidently supplies thromboplastin which neutralizes the excess of antithrombin according to Whipple. Prothrombin is then liberated and unites with calcium to form a clot around the traumatized blood vessels, and bleeding ceases.

The mothers exhibited a marked degree of debility since nearly two-thirds of them had an antepartum complication. This has not been recorded by previous writers. A greater frequency in colored women whose debility is generally recognized, was also seen. The average hemoglobin value was only 65 per cent. Poorer maternal health was further established by the greater incidence of postpartum morbidity.

In regards to the infants, prematurity was outstanding, with an incidence of 9.7 per cent. Immaturity was also frequently observed. The presence of nucleated red blood cells at birth, either on examination of a blood smear or on histologic section of the placenta, may be a better indication of prematurity even in apparently full-term infants. Several infants had an increased number of nucleated red blood cells. Losee has also found prematurity to be a factor in hemorrhagic disease. In this clinic McKee has shown that 4.5 per cent of 310 premature infants

colored race, and to the presence of debility of the mothers in the impoverished district which the Berwind Clinic serves. They had an average hemoglobin of only 69 per cent.

The more frequent use of drugs in the management of a confinement in the hospital seems to be important. Is the unknown toxin mentioned by Von Reuss as a cause of hemorrhagic disease actually a drug? A chronologic study of the use of drugs in obstetrics gives this view some support. Stearn in 1822 advocated ergot for the stimulation of labor. Its use was discontinued because of tetanic uterine contractions, and in 1875 Mullan recommended quinine instead. Watson in 1920 introduced castor oil, quinine, and pituitrin for stimulation of labor. Gwathmey in 1922 began the use of quinine and ether rectally as an obstetric analgesic. It is generally believed that quinine does not harm the mother or the infant. However, Gellhorn, Torland, and others have reported intrauterine deaths following the administration of quinine to the mother. In this series, quinine was given to 62.9 per cent of the mothers delivered in the hospital. No infantile deaths were attributed to the quinine.

Another group of drugs is bismuth and the arsenical preparations for the treatment of syphilis during pregnancy, which began in 1914 according to McKelvey. Antiluetic therapy was given to 5 mothers, 3 of whom were cared for on the outdoor service. Still another drug requiring consideration is ether, first introduced in 1847 by Simpson. It was administered either by inhalation or by rectum, or both, to a large number of the mothers. In addition many also received nitrous oxide. Webster in 1915 introduced this form of analgesia. Both have asphyxial properties. Ether has a dilating effect on the blood vessels. This relaxation allows more blood to enter the fetal circulation with each uterine contraction, resulting in engorgement and hyperemia. Did ether act in any way to produce the hemorrhagic lesions? An analogous drug, chloroform, was used by Graham with the production of hemorrhagic lesions in the unborn young of animals. Anoxemia was thought to have caused these ecchymoses. In our study, the addition of oxygen to nitrous oxide and ether anesthesia appeared to lower the incidence of hemorrhagic disease, whereas it was higher when nitrous oxide or ether was used alone. Further evidence of asphyxia is shown by the increased degree of resuscitation of the infants. Terplan believes that the hemorrhages noted in infants dying of asphyxia are produced by anoxemia.

The increased blood loss in the third stage may be further evidence of abnormal parturition. Many factors contributing to the increased blood loss were present. Postpartum hemorrhage was two and a half times more frequent, while the total average blood loss was 100 c.c. more than in the control. It can be inferred that some of the same factors causing excessive bleeding in the mothers probably influence the infants to bleed abnormally.

although erythroblastosis must be considered in the differential diagnosis. The presence of anemia, and the prolongation of the bleeding and clotting times are helpful when they are abnormal, although both were often within normal limits.

TREATMENT

The curative value of human blood in hemorrhagic disease is almost a specific; the beneficial substance is not known. There is reason to believe that it is thromboplastin. Mortality ranges from 50 to 84 per cent if blood therapy is not instituted, as is shown in Table IX. The blood is given intramuscularly or by transfusion. Welch in 1910 introduced the use of intramuscular serum, and Lambert in 1908 was one of the first to use transfusions.

In this series, 50 infants received transfusions of citrated blood, while 13 were given two or more transfusions. In this group the mortality rate was 14.2 per cent. Whole blood alone in the supposedly less severe cases resulted in no deaths. When whole blood and transfusion were used the mortality was 13.8 per cent. However, the mortality rate is not an accurate index of treatment, since the main causes of death were bronchopneumonia and intracranial hemorrhage. No attempt was made to correct the mortality rate, and the role of hemorrhagic disease in these cases can only be inferred.

The mother's blood was used for all the intramuscular injections, and for 21 of the transfusions. The mother is an undesirable donor. She is usually debilitated and anemic; she has often had a long or severe labor; has received drugs and anesthesia; and has usually sustained an increased blood loss in the third stage of labor. While the mother's blood evidently contains the curative agent, the concentration has been lowered by the physiologic hydremia of pregnancy as well as by the blood loss. In view of these facts the early puerperium (when these infants bleed) is an undesirable time to take blood from the mother to give to her infant.

Transfusion is not justified for all cases unless an anemia is present. To increase the intravascular tension at a time when capillary tissues have been injured by the forces of labor, does not seem logical and may cause the bleeding to continue. Over one-fourth of the cases required repeated transfusions. It is believed that the existing polycythemia and the congestion and hyperemia of the internal organs will not be enhanced by blood intravenously. Furthermore, the possibility of a co-existing intracranial hemorrhage in addition to the multiple lesions in the internal organs, makes transfusion undesirable unless an anemia or a markedly prolonged bleeding time makes it mandatory.

How then can these cases be treated adequately? The beneficial value of intramuscular blood has been shown in Table IX and in the publication of Capon. Welch has advocated blood serum and employed as much as 209 c.c. over a period of days. Many object to whole blood since the

developed clinical signs of hemorrhagic disease, whereas the incidence for full-term and premature infants is only 0.773 per cent.

Blood studies were not conclusive. The average bleeding time was prolonged to fourteen minutes while the clotting time was under ten minutes. After treatment of the disease circumcision was done during the second week of life in 7 of the cases. No increased bleeding was noticed. Apparently the bleeding tendency of infants during the first few days of life was known to the ancient Jews, for in St. Luke, Chapter II, verse 21, a definite period of time is given: "... and when eight days were accomplished for the circumcising of the child. . . ." Carr found that prolonged labor and operative deliveries did not increase the bleeding and clotting times. Lucas states that a clotting time of twenty to forty minutes can be present without hemorrhage. The blood platelets were present in adequate numbers. Several infants had an increased number of nucleated red cells. An anemia existed in nearly one-fourth of the infants. This was evidently a result of the bleeding in most of the cases. In others prematurity seemed to be the cause since primary anemia of the Ecklin type is a rarity. A hemolysin may be responsible for the anemia.

The sepsis theory of Epstein, Welch, and Townsend was not given credence in this study. Blood culture studies in our cases were not remarkable. Only 14 cases had fever, 5 of which had bronchopneumonia. Townsend noted fever in all but 2 of his 50 cases. In preaseptic days Von Reuss states that umbilical bleeding was a frequent symptom of sepsis.

Icterus was not more frequent, which is contrary to the findings of Keating, Minot, and Thayer, who explained the bleeding on accumulation of bile in the blood, thereby prolonging the bleeding time. Thayer found an absence or an impervious condition of the bile ducts in 32 per cent of his cases. In this series only one infant had an atresia of the common bile duct.

DIAGNOSIS

Clinical evidence of bleeding in the newborn infant has been the single criterion for the diagnosis of hemorrhagic disease. This is not sufficient, since it is necessary to differentiate it from: hemophilia, congenital syphilis, icterus gravis, purpura, erythroblastosis fetalis, traumatic bleeding, and spurious hemorrhage. This study has revealed the importance of maternal factors, such as antepartum complications, maternal debility, drugs before and during labor, long or severe labors, and the increased blood loss during the third stage of labor. Petechiae of the skin may be noted at birth, and many cases show spontaneous hemorrhages on the first day of life. Multiple lesions are often present. The child is often premature, or if of average weight, it has signs of immaturity. Nucleated red blood cells in the blood smear or in the fetal capillaries of the placenta are interpreted as evidence of prematurity,

9. The fetal factors were: immaturity and prematurity, the need for resuscitation indicating anoxemia, and the prolongation of the bleeding time.

10. The use of the mother as a blood donor is open to criticism.

11. Sedation and rest of the bleeding organs and the administration of intramuscular blood are important. Transfusion is indicated when these measures fail, or in the presence of anemia.

12. The total fetal mortality statistics show that 2.5 per cent of 439 neonatal deaths were due to hemorrhagic disease.

13. The fetal vessels of the placenta offer an excellent opportunity of studying the fetal blood at the time of delivery.

14. The same factors which cause excessive bleeding in the mothers, probably predispose the infants to abnormal bleeding.

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blood lost by the infant is not replaced. This view is not tenable since most of the infants did not have an anemia. Pooled serum when available would be ideal, together with sedation and rest of the bleeding organs. Schloss and Commiskey treated nine cases with human blood intramuscularly with a cure in 7 cases.

Prophylactically, intramuscular whole blood may have value in infants that have had an abnormal parturitional course. Heffernan gave whole blood to 800 consecutive infants to determine its value in intracranial hemorrhage. In these, no cases of hemorrhagic disease were observed, whereas at least 6 cases should have occurred.

SUMMARY

A study of 72 cases of hemorrhagic disease, occurring in 11,303 infants born during the period from September, 1932, to April, 1936, inclusive, has been presented. This comprises the material on the indoor and Outdoor Services of the Woman's Clinic of the New York Hospital. Emphasis has been placed on certain maternal and infantile factors. Criteria have been suggested for diagnosis. The treatment has been discussed and the autopsy data have been included.

Additional studies are indicated and should include: antepartum and intrapartum aspects of pregnancy; the use of drugs; further consideration of the blood loss in the third stage of labor; dietary factors; prematurity; blood studies, especially normoblastic determinations in the blood smears or in the fetal vessels of the placenta; blood pressure and blood volume determinations; capillary fragility tests; arterial oxygen; and the value of intramuscular whole blood.

CONCLUSIONS

1. The incidence of hemorrhagic disease is 0.773 per cent in the hospital, and 0.304 per cent in the outdoor service.
2. Parturitional factors are: prolonged or severe labor, anesthesia and analgesia, and increased blood loss during the third stage of labor.
3. Maternal debility, antepartum complications, and age appear to have an influence.
4. The intrauterine origin of hemorrhagic disease is more than probable.
5. Increased circulatory tension caused by the forces of labor may produce a separation of the capillary endothelial cells or actual rhexis of smaller blood vessels, thereby producing the multiple hemorrhagic lesions in the various organs, as were noted both clinically and pathologically.
6. The multiplicity of the lesions suggests that the condition is a generalized systemic process.
7. One-third of the cases began to bleed during the first twenty-four hours of life; only 2 cases had the onset of bleeding after the first week of life.
8. Bleeding precipitated by vascular trauma probably continues when the clotting or bleeding mechanism is abnormal.

term infant appear to be able to withstand the forces of normal labor. It is important to note that on no occasion in this series among the term infants was the premature type of lesion found. Tables III, IV, V, and VI summarize the premature infants coming to autopsy during the same period of time. It should be



Fig. 1.—Intracranial injury in term infant, delivered by forceps. Laceration of tentorium. Subdural hemorrhage.



Fig. 2.—Intracranial injury in premature infant. Spontaneous delivery. Diffuse subarachnoid hemorrhage and bilateral subventricular hematoma.

stated clearly that in the estimation of prematurity, more weight was placed on the statement of the mother as to the duration of pregnancy than upon the weight or length of the infant. Pregnancies at or over the thirty-eighth week were considered to be at term. The prematures coming to autopsy were divided into two groups, those born between the thirty-fifth and thirty-eighth week of pregnancy,

THE RELATION OF LABOR TO INTRACRANIAL INJURY IN THE PREMATURE INFANT*

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IN RECENT years a great deal of interest has been shown in injuries sustained by the fetus during labor and delivery. Most of the emphasis has been laid on the lesions sustained by the full-term infant and its relation to instrumental delivery and breech extraction. Less interest has been shown in the character, method of production, and prevention of injuries to the premature fetus. Berlind,¹ Galloway,² Capper,³ and Clifford,^{4, 5} have discussed the causes and prevention of these lesions. Hemsath⁶ has described them but appears to be at a loss as to their causation.

The pathologic lesions found at autopsy have been described by one of us in a previous article.⁷ The general character of these lesions is illustrated in Fig. 1, showing the dural lacerations and subdural hemorrhage which are found most commonly in the term infant. In addition microscopic hemorrhage may be found in the brain itself. Fig. 2 shows the lesions most characteristic of the premature which consist of diffuse subarachnoid hemorrhage, gross cerebral hemorrhage, and, in particular, subventricular hematomas. As we will show later there is no sharp division between these two groups since the premature infant past the thirty-fifth week commonly is found to have a combination of both types of lesion at autopsy.

The forces producing intracranial injury in the term infant are apparently much greater than those which cause injury in the premature.

Tables I and II show 20 cases of term infants coming to autopsy between July 1, 1933 and Feb. 28, 1936. It will be noted that in eleven cases the delivery was accomplished by midforceps operations and that in a majority of instances it was necessary to rotate the fetal head. On five occasions the injury occurred during breech deliveries. In one instance the fetus was delivered by version and breech extraction. In only three instances was an injury found after spontaneous labor. In two of these cases the labor was precipitate with strong uterine contractions. It is worthy of notice that in this series there was no case of intracranial injury following delivery with low forceps. It may be concluded that injuries in term infants are most likely to occur in difficult midforceps or high forceps deliveries commonly involving rotation of the fetal head or in breech extractions. A minority occur due to abnormally strong uterine forces. The cranial structures of the

*Read at combined meeting of Sections of Obstetrics and Gynecology and of Pediatrics, New York Academy of Medicine, February 11, 1937.

and those born before the thirty-fifth week. Table III summarizes 7 cases belonging to the first group. It will be noted that the majority showed a lesion of the type generally found in term infants, while a minority showed the premature type of lesion. In the majority of infants the forces of labor were not noted to be abnormal and the delivery was spontaneous. One may conclude that in this group the fetal head has become large enough to be subject to compression when opposed to resistant soft parts but that the intracranial supporting structures have not yet developed sufficiently to resist these forces. The arachnoid and cerebral vascular lesions are noted in a minority of instances. It will be noted that the last case in this group died of pneumonia at the age of sixty-nine days. Evidence of old cerebral hemorrhage was found at autopsy. This suggests that the premature may survive cerebral vascular injury sustained at birth. It is possible that this type of lesion may give rise to neurologic signs and symptoms in later life. Tables IV, V, and VI summarize the autopsies and clinical histories of 38 premature infants and stillbirths. These are taken in sequence without regard to viability. It will be noted that the vast majority of these cases showed arachnoid or subventricular hemorrhages, the incidence of dural lacerations and subdural hemorrhage being markedly reduced in this group. The more premature the infant the greater was the likelihood of the former type of lesion. Thirty-two of these cases occurred following spontaneous vertex delivery. Five cases occurred after assisted breech deliveries and one followed a low forceps in which no episiotomy was done. It must be apparent from these summaries that the connective tissue supporting structures and the blood vessels in the premature infant are not always strong enough to resist the normal forces encountered during labor and delivery. This tendency becomes more marked the greater the degree of prematurity. Capper³ believes that the vascular weakness depends on the lack of development of elastic tissue. Ylppö⁸ has shown experimentally that the cutaneous vessels in the premature are abnormally fragile. Using suction on the skin he found that hemorrhages occurred with a negative pressure of 150 mm. of mercury whereas 520 mm. of mercury were required to produce the same effect in term infants.

Granting that we are dealing with a fetus with inadequate connective tissue and vascular development, it is of interest to speculate on the point during parturition at which these injuries occur. The dural lacerations are easily explained on the basis of compression, first, by the dilating cervix during the first stage and, second, by the opposition offered by the perineal structures during the second stage. One would expect that premature rupture of the membranes would be an additional factor since an intact amniotic sac tends to equalize intrauterine forces during the first stage. The exact cause of the vascular lesions is more difficult to determine. It must be supposed that the fetus is under a marked increase of pressure during the uterine contractions. The portion of the fetal head exposed in the dilating cervix or in the vaginal introitus becomes an area of relatively low pressure. In the second stage the expulsive forces are increased by the voluntary efforts of the patient. This pressure relationship is reflected to the intracranial structures. As a result the blood vessels in the area of relatively low pressure become distended. If distention is pronounced

TABLE I. TERM BABIES WITH HEAD INJURIES 20 CASES, JULY 1, 1933 TO FEB. 28, 1936

NAME ACCESSION NUMBER	WEIGHT	DURAL LACERA- TION	SUB- DURAL HEMOR- RHAGE	METHOD OF DELIVERY	AGE	APPEAR- ANCE AT BIRTH	LENGTH OF GESTATION	LENGTH OF LABOR HOURS	DRY HOURS	PELVIS	PARITY
Mrs. F. 19453	3390	+	+	Breech	5 min.	Poor	40	3	25½	Transverse contraction of outlet Ample	Para 0 Grav. i
Mrs. L. 19571	2910	+	+	Spontaneous	S/B		40	11½	½	Ample	Para ii Grav. iii
Mrs. M. 19702	3640	+	+	Midforceps	S/B		40	68	68	Ample	Para 0 Grav. i
Mrs. S. 20451	3196	+	+	Barton midforceps R.O.T.	S/B		40	6½			
Mrs. O. 20666	3310	+	+	Precipitate with im- pacted shoulders	S/B		40	25	11	Ample	Para ii Grav. iv
Mrs. Mc. 20733	3064	+	+	Breech	6 min.	Poor	40	21½	20	Anthropoid	Para 0 Grav. i
Mrs. M. 22059	4100	+	+	Midforceps Kieland R.O.T.	S/B		40	16	2	Gynecoid	Para 0 Grav. i
Mrs. M. 21415	3270	+	+	Midforceps Haig Ferguson LOP—Toxemia	3 days		40	26½	10	Gynecoid	Para 0 Grav. i
Mrs. M. 21339	3190	+	+	Spontaneous Lac. of cervix. Very strong pains	S/B		40	8½	½	Gynecoid	Para v Grav. vi
Mrs. S. 21243	3190	+	+	Mid A Kieland R.O.P.	S/B		40	1	15	Gynecoid Android tendency	Para 0 Grav. i
Mrs. F. 21091	4772	+	+	Barton, high forceps L.O.T.	S/B		40	5	6½	Android	Para viii Grav. ix
Mrs. C. 20983	3190	+	+	Version and breech after attempted high forceps R.O.T.	S/B		40	36	5	Anthropoid	Para ii Grav. iii
Mrs. M. 20944	3490	+	+	Vertex R.O.P. Kieland high forceps	S/B		40	18½	5	Flat pelvis	Para 0 Grav. i

TABLE V. HEAD INJURIES IN BABIES UNDER THIRTY-FIVE WEEKS' GESTATION, 38 CASES, JULY 1, 1933 TO FEB. 28, 1936

NAME ACCESSION NUMBER	WEIGHT	DURAL LACERA- TION	SUB- DURAL HEMOR- RHAGE	SUB- ARACH- NOID HEMOR- RHAGE	CERE- BRAL AND VENTRICULAR HEMOR- RHAGE	METHOD OF DELIVERY	AGE HOURS	APPEAR- ANCE AT BIRTH	GESTA- TION WEEKS	DURA- TION OF LABOR HOURS	DRY HOURS	PELVIS	PARITY
Mrs. Mc. 19378	2260	+	+	+		Spont. vertex	16	Poor	32	6	26 hr.	Not esti- mated	Para 0
Mrs. B. 19382	1520	+	+	+		Spont. vertex	21	Poor	32	12	72 hr.	Clinically ample	Grav. i Para ii
Mrs. C. 19431	1900				+	Spont. vertex	14	Poor	28	6	5 min.	Ample	Grav. iii Para 0
Mrs. S. 19460	1010	+	+			Spont. vertex	9	Cyanosis	33	17½	24½ hr.	Ample	Grav. i Para 0
Mrs. N. 19497	520			+		Spont. vertex	½	Poor	25	14	21 hr.	Ample	Grav. i Para 0
Mrs. D. 19524	1845			+		Spont. vertex	4	Poor	31	23	½ hr.	Ample	Grav. i Para 0
Mrs. G. 19672	730	+	+			Assisted breech	S/B		24	4½	60 hr.	Not esti- mated	Grav. i Para 0
Mrs. G. 19677	2215	+	+			Spont. vertex	11	Cyanotic	33	28½	28½ hr.	Not esti- mated	Grav. i Para ii
Mrs. R.-A 19736	1035				+	Spont. vertex	8	Poor	25	52½	0	Ample	Grav. iii Para i
Mrs. R.-B 19742	935				+	Spont. vertex	4	Poor	25	54½	0	Ample	Grav. ii Para i
Mrs. G. 19762	1185			+		Spont. vertex	1	Poor	28	1	½ hr.	Not esti- mated	Grav. ii Para 0 Grav. i

TABLE IV. HEAD INJURIES IN BABIES UNDER THIRTY-FIVE WEEKS' GESTATION—38 CASES—JULY 1, 1933—FEB. 28, 1936

NAME ACCESSION NUMBER	WEIGHT	DURAL LACERA- TION	SUB- DURAL HEMOR- RHAGE	SUB- ARACH- NOID HEMOR- RHAGE	CERE- BRAL AND VENTRIGULAR HEMOR- RHAGE	METHOD OF DELIVERY	AGE HOURS	APPEAR- ANCE AT BIRTH	GESTA- TION WEEKS	DURA- TION OF LABOR HOURS	DRY HOURS	PELVIS	PARITY
Mrs. G. 19939	1060	+	+			Assisted breech	12	Poor	30	8	0	Not esti- mated	Para 0
Mrs. R. 19942	1021			+	+	Assisted breech	1	Poor	31	14	0	Ample	Grav. i Para i
Mrs. M. 19951	2383			+	+	Spont. vertex	2	Fair	32	24	?	Ample	Grav. ii Para iii
Mrs. T. 20037	1580	+	+			Breech	8	Poor	26	7	2	Not esti- mated	Grav. v Para 0
Mrs. O. 20576	2043		+	+	+	Spont. vertex	4	Fair	34	28½	0	Ample	Grav. i Para 0
Mrs. G. 20584	1135			+	+	Spont. vertex	5	Fair	28	6	8½	Generally contracted	Grav. i Para i
Mrs. S. 20652	908			+	+	Spont. vertex	S/B		24	22	120	Ample	Grav. ii Para iv
Mrs. S. 20836	1660		+			Spont. vertex	5	Poor	32	1½	?	Ample	Grav. vii Para vi
Mrs. V. 20882	1900			+		Spont. vertex	4	Poor	31	5½	36	Ample	Grav. vii Para i
Mrs. L. 20930	1660			+		Spont. vertex	11	Poor	34	7	3	Ample	Grav. ii Para 0
Mrs. F.-B 21122	570		+	+		Spont. O.P.	4	Poor	28	3½	0	Not esti- mated	Grav. i Para 0
Mrs. F.-A 21123	690		+		+	Spont. vertex	S/B		28	3	0	Not esti- mated	Grav. ii Para 0
Mrs. B. 21428	1690			+		Spont. vertex	9	Good	28	4	18	Not esti- mated	Grav. ii Para i
Mrs. H. 21848	700			+		Spont. vertex	12	Poor	24	0	24	Not esti- mated	Grav. ii Para 0
Mrs. F. 21899	795			+		Assisted breech	1½	Poor	25	8	½	Not esti- mated	Grav. i Para i
Mrs. L. 21966	600				+	Spont. vertex	S/B		25	36	0	Not esti- mated	Grav. ii Para iv
Mrs. C.-A 22076	390			+		Spont. vertex	S/B		23	8	1	Not esti- mated	Grav. v Para 0
Mrs. C.-B 22077	360			+	+	Spont. vertex	S/B		23	8	1	Not esti- mated	Grav. iii Para 0

these vessels burst. Distention reflected backward along the dural sinuses through the great cerebral vein would account for the rupture of the weak tributary vessels beneath the floor of the lateral ventricles. A common result of the same forces in the term infant is the caput succedaneum which on section always shows a hemorrhagic edema. This explanation is very similar to that offered by Abels⁹ in 1913.

In order to determine more clearly the effect of labor and the method of delivery in the premature infant, 249 consecutive cases occurring between June 1, 1934 and June 1, 1936 were studied. Tables VII and VIII show the relationship of prolonged labor, with and without ruptured membranes, to the incidence of intracranial injury in those stillbirths and infants who came to autopsy. Among the primiparas there is a very definite trend to an increased incidence of injury in prolonged labor and a less definite one in the cases of dry labor. On the other hand among the multiparas, the figures do not permit any conclusion to be drawn.

This series of premature infants was delivered by a number of different methods. The group was broken up according to the various techniques employed. Spontaneous delivery of the premature infant occurred in 153 cases. Table IX shows the result in 57 cases occurring in primiparas. Allowing for certain corrections, eliminating macerated fetuses, anencephalics, and those cases not coming to autopsy, it was

TABLE VII. RELATION OF DURATION OF LABOR AND OF DRY LABOR TO OCCURRENCE OF INTRACRANIAL SURGERY IN PREMATURES BASED ON AUTOPSIES

PRIMIPARAS

DURATION OF LABOR; HOURS	LABOR			DRY LABOR		
	NO INJURY	INJURY	% INJURED	NO INJURY	INJURY	% INJURED
5	10	2	16.1	14	9	39.1
10	6	2	25.0	2	3	60.0
15	2	2	50.0	1	0	0
20	1	4	80.0	1	3	75.0
30	1	3	75.0	0	0	0
40	3	1	25.0	2	0	0

TABLE VIII. RELATION OF DURATION OF LABOR AND OF DRY LABOR TO OCCURRENCE OF INTRACRANIAL SURGERY IN PREMATURES BASED ON AUTOPSIES

MULTIPARAS

DURATION OF LABOR; HOURS	LABOR			DRY LABOR		
	NO INJURY	INJURY	% INJURED	NO INJURY	INJURY	% INJURED
5	10	9	47.3	15	8	34.7
10	3	3	50.0	0	0	0
15	3	0	0	1	1	50.0
20	2	1	33.3	0	0	0
30	1	0	0	0	0	0
40	0	0	0	1	1	50.0

TABLE VI. HEAD INJURIES IN BABIES UNDER 35 WEEKS' GESTATION, 38 CASES, JULY 1, 1933 TO FEB. 28, 1936

NAME ACCESSION NUMBER	WEIGHT	DURAL LACERA- TION	SUB- DURAL HEMOR- RHAGE	SUB- ARACH- NOID HEMOR- RHAGE	CERE- BRAL AND VENTRICULAR HEMOR- RHAGE	METHOD OF DELIVERY	AGE	APPEAR- ANCE AT BIRTH	GESTA- TION WEEKS	DURA- TION OF LABOR HOURS	DRY HOURS	PELVIS	PARITY
Mrs. C. 22087	960				+	Spont. vertex	S/B		26				
Mrs. L. 21360	1700	+	+	+		Spont. vertex	8 days	Fair	30	3	1	Ample	Para 0 Grav. i
Mrs. S. 21530	1900			+		Spont. vertex	8 days	Fair	28	15	18	Not esti- mated	Para 0 Grav. i
Mrs. A. 22358	1200	+	+			Assisted breech	3 hr.	Poor	30	5½	0	Ample	Para ii Grav. iii
Mrs. M. 22617	1700	+	+	+		Forceps low No epis- iotomy	4 hr.	Good	30	15½	0	Ample	Para 0 Grav. i
Mrs. Z. 22633	1550		+	+	+	Spont. vertex	6 hr.	Poor	29	62	61	Ample	Para 0 Grav. i
Mrs. S. 22920	850		+	+	+	Spont. vertex	9 days	Fair	31	3		Not esti- mated	Para i Grav. vi
Mrs. M. 22927	1250				+	Spont. vertex	3 hr.	Poor	28	10	28	Ample	Para i Grav. iii
Mrs. D. 22946	800		+		+	Spont. vertex	4 hr.	Fair	25	22½	48	Not esti- mated	Para ii Grav. iv

an intracranial injury. Five were in multiparas and no traumatic lesions were found in 3 infants who came to autopsy. Of the remaining patients 30 delivered as breech presentations, and 6 by cesarean section. Time does not permit the presentation of these tables. However, it was found, particularly in the primiparas, that intracranial injury was less likely to occur when an episiotomy was performed before delivering the aftercoming head. These figures suggest that, while injury may occur during the first stage, more commonly it is produced in the second stage of labor, and that it occurs more commonly when the mother is a primigravida. If this is the case, the incidence of these lesions can be markedly reduced by certain procedures. The problem of the care of the premature infant is not only confined to the neonatal period but also concerns the intrapartum period. It is felt that the obstetrician can, with proper care, diminish the number of handicapped infants who are passed over into the hands of the pediatrician.

In closing it seems worth considering how these injuries may be minimized. Prevention of these injuries involves two considerations.

TABLE XI. PRIMIPARAS

Spontaneous vertex delivery with episiotomy	8
Total stillbirths and neonatal deaths	3
Correction	0
Intracranial injury found at autopsy	0
Percentage	0%

TABLE XII. PRIMIPARAS

Forceps delivery with episiotomy	31
Total stillbirths and neonatal deaths	4
Correction	0
Intracranial injury found at autopsy	0%

TABLE XIII. PRIMIPARAS

Forceps delivery without episiotomy	3
Total stillbirths and neonatal deaths	2
Intracranial injury found at autopsy	1
Correction—no autopsy	1
Percentage of intracranial injury found at autopsy	100%
Percentage intracranial injuries in prematures delivered with low forceps without episiotomy	50%

TABLE XIV. MULTIPARAS

Vertex—forceps delivery without episiotomy	5
Total stillbirths and neonatal deaths	3
Correction—not autopsied	1
Total autopsied prematures considered	2
Intracranial injury found at autopsy	0

found that 62.5 per cent of the autopsied cases showed intracranial injury and that the incidence of this lesion in the entire group was 34.8 per cent. Table X shows the results in 96 cases occurring in multiparas. Again allowing for the same corrections, it was found that 44 per cent of the autopsied cases showed intracranial lesions, while the incidence of these injuries for the group was 14.4 per cent. The marked difference in incidence of intracranial injury following primiparous labors as compared to multiparous labors suggests strongly that many of these injuries may occur during the second stage of labor and that they are due to the greater resistance offered by the perineal structures in the former type of patient.

TABLE IX. PRIMIPARAS

Spontaneous vertex deliveries without episiotomy	57	
Total stillbirths and neonatal deaths	38	(66%)
Macerated fetus; no autopsy; anencephalic	14	
Total autopsied prematures considered	24	
Intracranial injuries found at autopsy	15	(62.5%)
Total of prematures considered	43	
(Excluding macerated fetuses, anencephalics and cases not autopsied)		
Percentage of intracranial injury in prematures delivering spontaneously without episiotomy	34.8%	

TABLE X. MULTIPARAS

Vertex—spontaneous without episiotomy	96	
Total stillbirth and neonatal deaths	45	(47%)
Macerated fetus; no autopsy; anencephalic	20	
Total autopsied prematures considered	25	
Intracranial injury found at autopsy	11	(44%)
Total of prematures considered	76	
(Excluding macerated fetuses, anencephalics; and cases not autopsied)		
Percentage of intracranial injury in prematures delivering spontaneously without episiotomy	14.4%	

A second group of vertex presentations was found in which the second stage had been shortened by various procedures. Table XI shows the results in spontaneous delivery in 8 primiparas following episiotomy. Three stillbirths and neonatal deaths occurred in this group. No intracranial injuries were found in those prematures who came to autopsy. No such group was found among the multiparas. Table XII shows the results of forceps delivery with episiotomy in 31 primiparas. Four stillbirths and neonatal deaths occurred. Again no intracranial injuries were discovered in those prematures who came to autopsy. No instance was found in which this procedure was used on a multiparous patient. Tables XIII and XIV show the results in 8 cases delivered by low forceps without episiotomy. Three were in primiparas. Only 1 infant survived, and of the 2 lost, 1 came to autopsy and showed

The Simpson type of forceps is best adapted to this type of delivery owing to its wide cephalic curve. This procedure is of particular value if the perineal structures offer marked resistance. It is believed that the routine use of this maneuver will result in a marked reduction of intracranial injuries in the premature infant.

Finally, efforts to restrain the premature fetal head by manual pressure in order to avoid a precipitate delivery or because an attending physician is not present, should be avoided. In the premature such efforts may result in intracranial injury.

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768 PARK AVENUE

INTERNAL PELVIMETRY AS A BASIS FOR THE MORPHOLOGIC CLASSIFICATION OF PELVES

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THE work of Caldwell and Moloy¹ shows that much useful information can be gained by studying the morphology of the pelvis as a whole in a purely descriptive qualitative way. This approach to the study of the subject, however, does not lessen the importance of quantitative methods; on the contrary, it gives promise of increasing the practical value of pelvic measurements by providing a more scientific basis for pelvimetry. Conversely, methods of precision simplify and increase the usefulness of morphologic classifications.

The aim of the present study is to assemble the most practical methods available for the measurement of the important classical diameters of the pelvis, and to supplement these with new methods for the measurement of the dimensions which the recent contributions of Caldwell and his associates have brought to light. The dimensions selected for measurement are those which are of greatest significance in the morphologic classification of Thoms,² and of Caldwell and Moloy.¹ A special effort is made to facilitate the recognition of male or android characters.

The first, the avoidance of unnecessary induction of labor. The second, the elimination of excessive compression in the second stage. Let us consider the first stage of labor.

Many cases of premature labor are initiated by rupture of the membranes. Because of the unwarranted fear of amniotic sac infection, it is a common practice to induce labor in such cases and to perform rectal or vaginal examinations at frequent intervals to determine the character of the cervix. If such a patient has a soft, retracted and partially dilated cervix, she will go into labor inevitably within twenty-four hours. If, on the other hand, the cervix is closed, firm, and unretracted, it is possible that pregnancy may proceed for several days or even weeks before labor begins. Induction in this type of patient, on the other hand, often produces a protracted first stage. An amniotic sac infection seldom occurs in a patient who is not in labor unless organisms are carried into the cervix or lower uterine segment by the examining finger, either vaginally or rectally. The protection of the sac probably depends on the constant formation and leakage downward of amniotic fluid and the presence of a closed unretracted cervix. When such a patient goes into spontaneous labor, it is frequently found that the cervix is adequately prepared and the duration of the process is usually short. This method of dealing with patients who have premature rupture of the membranes has been a routine practice at Bellevue Hospital for the past three years. Only one instance of amniotic sac infection has been observed among these patients treated by simple bed rest. This occurred in a patient who was examined vaginally under the mistaken impression that she had begun labor. It is believed that this policy will often allow the patient to continue pregnancy to a point closer to term and that it will terminate in a shorter, easier labor. Both of these results will reduce the incidence of intracranial injury.

The induction of premature labor in the presence of resistant soft parts in order to bring a small fetus through a borderline pelvis is to be condemned. An induced labor is frequently prolonged and the premature infant often sustains injuries during the process.

Of even greater importance is the conduct of the second stage of labor. During this period it is possible to definitely shorten the process and to reduce the forces to which the premature is exposed, particularly in the primiparous patient. This can readily be done by anesthetizing the mother and delivering the fetus by low forceps and episiotomy. Voluntary efforts on the part of the mother in the presence of resistant soft parts are to be discouraged. A cephalic application of forceps is of even greater importance than in the term infant.

mined by fitting a gauge between the pubic rami at a perpendicular distance of 3.0 cm. below the inferior border of the symphysis pubis (Fig. 2). Five-tenths centimeter is added to the reading obtained to compensate for the thickness of the soft tissues covering the pubic rami.

The width of the subpubic angle in the last 100 consecutive cases, as determined in this manner, was found to vary between 95 degrees and 132 degrees (average 107 degrees). A subpubic angle of 100 degrees or less may be regarded as an android character. There were 8 cases in the present series in which the subpubic angle was contracted to this degree.

THE DIMENSIONS OF THE NARROW PELVIC PLANE

The plane of least dimensions, or narrow pelvic plane has been defined as the level of the pelvis which is bounded anteriorly by the lower border of the symphysis pubis, laterally by the ischial spines, and posteriorly by the tip of the sacrum. These three points are, however, not truly in the same plane, since the tip of the sacrum is approximately 2 cm. below the level of a line joining the apex of the pubic arch with the bispinous diameter. Furthermore, measurements taken from the tip of the sacrum are at too low a level to serve as an index of the sagittal dimensions of the mid, and upper posterior pelvis.¹ In the present study the junction of the fourth and fifth sacral segments is therefore selected to represent the posterior limit of the narrow pelvic plane. By raising the posterior boundary even by as little as one sacral segment a more representative picture is obtained of the width of the sacrosciatic notch, and of posterior pelvic capacity. This is of great importance in the recognition of the android pelvis.¹

Other significant essentially android characters, according to my own observations, are the contracted bispinous and interischial diameters, and the narrow retropubic angle.

Methods for the measurement of these important dimensions of the narrow pelvic plane are presented in the sections to follow.

THE TRANSVERSE DIAMETERS OF THE NARROW PELVIC PLANE

My interest has long been focused on the bispinous and interischial diameters. In previous communications^{3, 4} I submitted methods for the measurement of these diameters. For the sake of completeness a description of these methods is again presented in abbreviated form. The procedure for the measurement of the bispinous diameter is briefly as follows:

The blades of the pelvimeter (Fig. 3) are separated. "The tip of the middle finger of the right hand is inserted into the ring of the vaginal blade (V). With the blade in place the index and middle fingers are

THE PELVIC OUTLET

The narrow subpubic angle has long been recognized as the most important character of the contracted pelvic outlet. Its width can be computed from the length of the anterior sagittal and transverse diameters of the outlet. There are, however, two sources of error in this method: First, the intertuberos diameter cannot be measured accurately, due to the variable thickness of the fat pad which covers the

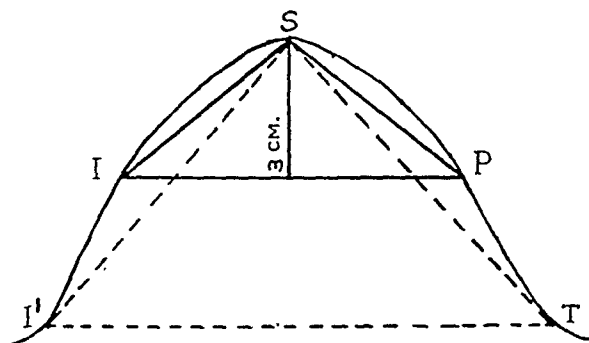


Fig. 1.—The pubic arch: *I'T.*, Intertuberos diameter; *I.P.*, interpubic diameter; *I.S.P.*, subpubic angle.

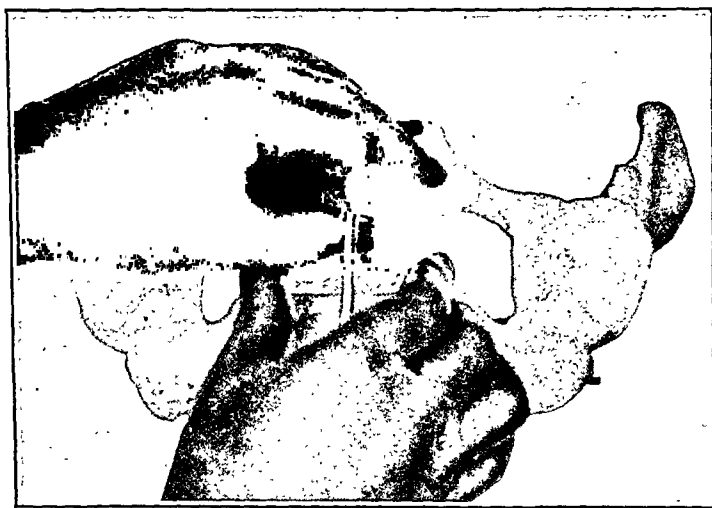


Fig. 2.—The measurement of the interpubic diameter. A gauge is fitted between the pubic rami at a distance of 3.0 cm. below the apex of the pubic arch. This distance is determined with the rectal blade of the internal pelvimeter.

tuberosities of the ischia. Second, the lateral curvature of the ischio-pubic rami is overlooked if the subpubic angle is estimated with the ischial tuberosities forming the base of the triangle (Fig. 1). Both of these sources of error can be minimized by selecting a point nearer to the pubic arch to form the base of the triangle from which the subpubic angle is to be computed. A point 3 cm. below the apex of the pubic arch was arbitrarily selected for this purpose. The transverse dimension of the outlet at this level will be designated as the interpubic diameter (Fig. 1). The width of the interpubic diameter can be readily deter-

The length of the anterior sagittal diameter is derived from values obtained by direct measurement of the bispinous and spinopubic diameters (Fig. 4). The length of the posterior sagittal diameter is determined by subtracting the value of the anterior sagittal from that of the sacropubic diameter.

For the measurement of the spinopubic diameter the vaginal blade is attached to the rectal blade in the reverse position (Fig. 5). The tip of the left index finger is passed into the ring of the rectal blade, and the blade resting on the dorsum of the finger is introduced into the rectum. The left ischial spine is identified and the ring is steadied against its tip while the lower border of the ring of the vaginal blade, held between the thumb and index finger of the other hand, is brought

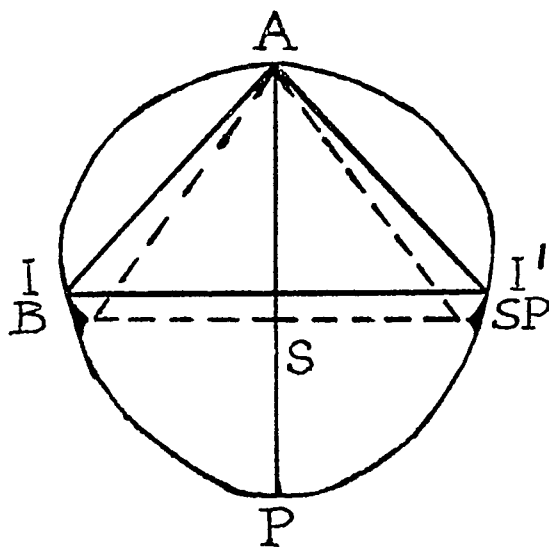


Fig. 4.—The diameters of the narrow pelvic plane: *B.SP.*, bispinous diameter; *A.SP.*, spinopubic diameter; *A.S.*, anterior sagittal diameter; *P.S.*, posterior sagittal diameter; *I.I'*, interischial diameter; *I.A.I.*, retropubic angle.

up against the inferior border of the symphysis pubis. A reading is made on the scale while the rings are held in this position.

The sacropubic diameter is measured in a similar manner, as previously described.⁵ The reading is taken while the ring of the rectal blade is held against the sacrum at the junction of the fourth and fifth segments, while the ring of the vaginal blade is brought up against the inferior border of the symphysis pubis. The junction of the fourth and fifth sacral segments is located by advancing the rectal ring internally along the sacrum until the distal interphalangeal joint of the finger carrying the ring comes to rest on the tip of the sacrum. The ring is thus placed at a distance above the tip of the sacrum equal in length to the length of the terminal phalanx of the index finger (about 2 cm.), which is approximately the junction of the fourth and fifth sacral segments. This localization is sufficiently accurate for all practical purposes.

introduced into the vagina. The tip of the index finger of the left hand is similarly placed within the ring of the rectal blade (*R*), and is introduced into the rectum. The two blades are now locked and the spinous processes are identified. The rings are then steadied against the tips of the spinous processes, and a reading is made on the scale."³ The interischial diameter is measured similarly, with the exception that the rings are carried anteriorly to the bases of the ischial spines when the reading is taken.

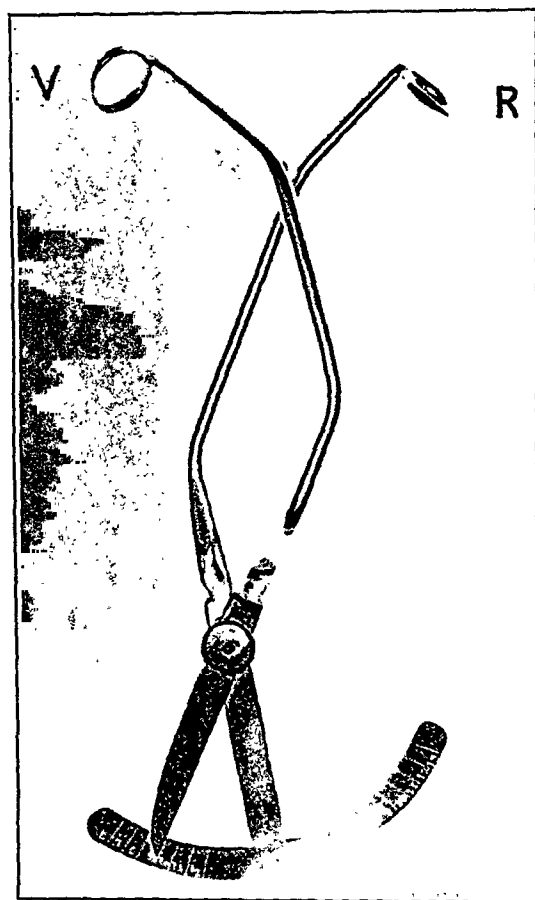


Fig. 3.—The internal pelvimeter: *R.*, rectal blade; *V.*, vaginal blade.

Statistical data on the bispinous and interischial diameters were presented in a previous report.⁴ Values for these diameters of 9.5 cm. and 10.0 cm., respectively, may be regarded as the lower limits of normal.

SAGITTAL DIAMETERS OF THE NARROW PELVIC PLANE

Early in the course of studies on the transverse diameters of the narrow pelvic plane my attention was drawn to the sagittal diameters. In 1932 I took measurements of these diameters in selected cases, but failed to appreciate their full significance. The recent work of Caldwell and Moloy stimulated my interest in the subject, and prompted me to devise simple and accurate methods for the measurement of the diameters under consideration.

inner border of the pubis, and the space between the fourth and fifth lumbar vertebrae, as in Thoms' original method.

The important android characters of the pelvic inlet, according to Caldwell and Moloy, are the short posterior sagittal diameter, the relatively long straight anterior puboiliac portions, and the narrow retro-pubic angle. These characters can be readily determined quantitatively on a Thoms film (Fig. 6). A posterior sagittal diameter of 3.5 cm. or less may usually be regarded as distinctly android.

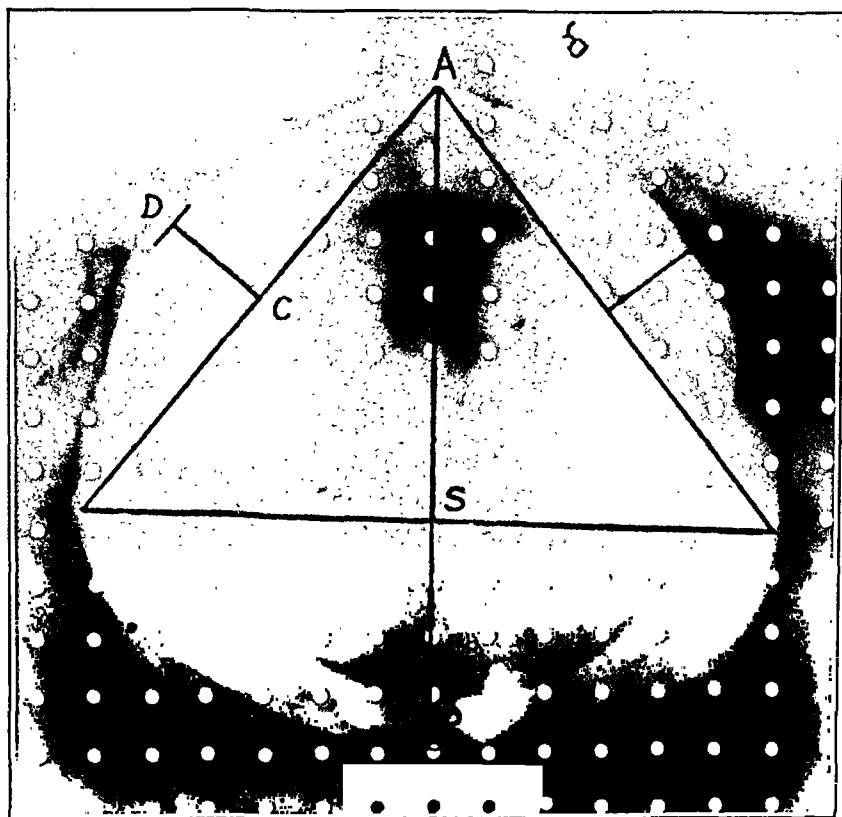


Fig. 6.—The dimensions of the pelvic inlet: *T.R.*, transverse diameter; *P.S.*, posterior sagittal diameter; *T.A.R.*, retro-pubic angle; *D.C.*, degree of curvature of anterior puboiliac portion.

THE MORPHOLOGIC CLASSIFICATION OF Pelves

The recent contributions of Caldwell and his associates mark a distinct advance in our knowledge of the android pelvis. The android characters to which these observers call attention are clear-cut, and unmistakable. This, however, cannot be said of the other three types in their classification. The identification of the gynecoid, anthropoid and platypelloid types can be made with certainty only from a study of the contour of the pelvic inlet. The differentiation of these three types at lower levels of the pelvis is confusing and tends to detract from the significance of the android characters which are often present in all these forms, and which deserve a place of greatest prominence in any classification. For practical purposes it may therefore be advantageous

The length of the sagittal diameters of the narrow pelvic plane was determined in the manner described in a series of 100 consecutive cases. The spinopubic diameter measured from 7.3 cm. to 9.4 cm. (average 8.30 cm.). The length of the anterior sagittal diameter was found to vary between 4.7 cm., and 7.4 cm. (average 6.48 cm.), and that of the posterior sagittal between 3.5 cm. and 8.0 cm. (average 5.59 cm.). In 19 cases the posterior sagittal diameter was longer than the anterior sagittal. A posterior sagittal diameter of 4.5 cm. or less may be regarded as an android character. There were 8 such cases in the present series.



Fig. 5.—Measurement of the sacropubic diameter. Vaginal blade reversed. Ring of rectal blade placed at junction of fourth and fifth sacral segments, while ring of vaginal blade is brought up against the inferior border of the symphysis pubis.

THE DIMENSIONS OF THE PELVIC INLET

Thoms' x-ray method⁶ was found to be satisfactory for the measurement of the dimensions of the inlet. The following minor modification was made to simplify the procedure:

An ordinary level is substituted for the plump-bob in estimating the height of the upper border of the pubis from the x-ray table. In so doing the interference of a protruding abdomen is avoided. The grid is adjusted to the proper height from points representing the upper

of asymmetric pelves, and to all cases where disproportion may be suspected, especially in primiparas at term with no engagement of the presenting part, and in multiparas with a history of previous complicated labors.

SUMMARY

Instrumental procedures of internal pelvimetry are supplemented by Thoms' x-ray method to provide quantitative data for the morphologic classification of pelves. Special emphasis is placed on android characters.

The width of the subpubic angle is computed from modified measurements of the anterior sagittal and transverse diameters of the outlet.

The bispinous and interischial diameters, and the anterior and posterior sagittal diameters of the narrow pelvic plane, are measured by means of an internal pelvimeter previously described which was especially designed for this purpose.

The diameters of the pelvic inlet are determined on a Thoms film. The dimensions measured are the transverse and the anterior and posterior sagittal diameters. The retropubic angle and the degree of curvature of the anterior puboiliac portions are also determined.

A morphologic classification of pelves is presented which is based on the classification of Thoms, and of Caldwell and Moloy.

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1009 MEDICO-DENTAL BUILDING.

ADDENDUM

The Posterior Sagittal Diameter of the Midplane.—As stated above, the posterior sagittal diameter at higher levels of the pelvis is an accurate index of the width of the sacrosciatic notch, and of posterior pelvic capacity. The determination of the length of the posterior sagittal diameter of the midplane is therefore desirable. This can readily be accomplished as follows:

The patient is placed on the side, and a point is marked on the sacrum equidistant from the lumbosacral interspace and the tip of the sacrum. The patient is then placed in the lithotomy position with the buttocks well over the end of the table. With an ordinary external pelvimeter a measurement is taken from the lower border of the symphysis pubis to the point marked on the sacrum. The thickness of the sacrum and overlying soft tissues is determined with the same pelvimeter by placing the tip of one arm of the instrument against the sacrum internally through

to give a subordinate place to the anthropoid and platypelloid forms, and to regard these merely as varieties of the gynecoid type.

The following is a simple morphologic classification of pelves based on the classifications of Thoms,² and of Caldwell and Moloy.¹

1. *Gynecic (JIN-E'SIK) Pelves:*

- (a) Mesatipellic (round)
- (b) Dolichopellic (oval); sagittal diameter of inlet longer than transverse diameter.
- (c) Brachypellic (oval); sagittal diameter of inlet shorter than transverse diameter.
- (d) Platypellic (flat); sagittal diameter of inlet excessively shorter than transverse diameter.
- (e) Asymmetric

2. *Android Pelves.*

The term "gynecic" (pertaining to women) is preferable to the term "gynecoid" which literally refers to the male pelvis with female characters.

The terms mesatipellic, dolichopellic, brachypellic, and platypellic are used only with reference to the pelvic inlet, in accordance with Thoms' definitions.² It is, however, assumed, unless otherwise stated, that the lower pelvis in these forms possesses essentially normal female characters.

The various gynecic types may have android abnormalities at the inlet, midpelvis or outlet; and conversely, the android pelvis may have gynecic characters at various levels. The mixed forms may be classed as android-gynecic or gynecic-android, depending on whether the male characters predominate at the pelvic inlet or at lower levels of the pelvis, respectively.

A subdivision of the above pelvic types into large, medium and small may be made, but such a subgrouping should be supplemented with quantitative data for all the important dimensions of the pelvis.

A careful morphologic classification of pelves is desirable in most cases. The expense of routine x-ray pelvimetry is, however, still considered prohibitive in most clinics. For the present, x-ray measurements must, therefore, be limited to selected cases. Internal instrumental pelvimetry may serve as a guide to the selection of cases for x-ray study. For practical purposes, a pelvis may usually be regarded as normal or gynecic, on the basis of clinical findings alone, when the promontory of the sacrum cannot be reached (C.D. of 12+), and when the subpubic angle, and the posterior sagittal and transverse diameters of the narrow pelvic plane are within normal limits. X-ray pelvimetry, however, becomes indispensable when a contraction is found in any one of these important dimensions. Under such circumstances all the diameters of the pelvic inlet must be accurately determined, and an absolutely correct diagnosis of the pelvic type must be made. The same applies to all forms

The only book found that differs from the above mentioned ideas is the 1890 English translation of Winckel's of the University of Munich. In this book it is stated: "The lungs are dragged apart, but the vital capacity is not interfered with, for Kuckenmeister, Fabins, Wintrich, and more recently Vejas (in my clinic) have not been able to find any such change, even in the last month. . . . Gerhardt, in forty-two cases, found the *diaphragm* higher than usual in one case only; in thirty-six its position was normal."

Since artificial pneumothorax and phrenic nerve interruption have become popular in the treatment of pulmonary tuberculosis, one of the arguments frequently given for the conservation of pregnancy in a tuberculous patient is that the gravid uterus elevates the diaphragm and acts as a splint, thus giving the effect of a phrenic palsy or pneumothorax. This hypothesis has been used as an argument that pregnancy would be as beneficial to the pulmonary lesions as a bilateral section of the phrenic nerves. It has also been used in the suggestion that after delivery of a tuberculous woman, the phrenic nerves should be sectioned to maintain the paralysis of the diaphragm that was supposed to have existed during the latter months of pregnancy.

The basis of this argument has been expressed by Professor Sergent⁹ of France as follows: "The apparent improvement that is observed during the latter months of pregnancy is due to the upward displacement of the diaphragm, thus creating a sort of bilateral artificial pneumothorax." Professor Crockett¹⁰ of St. Mungo's College, Glasgow, in 1934 stated: "When a female who is suffering from tuberculosis becomes pregnant, there is produced an increasing intra-abdominal pressure. This acts on the lung exactly like an artificial pneumothorax or a phrenic avulsion operation, which causes paralysis of the diaphragm and causes the diaphragm to rise up into the thoracic cavity."

Our observations from the fluoroscopic examination of pregnant patients did not agree with the viewpoint that the gravid uterus splints the diaphragm. Our fluoroscopic observations did agree with the observations of Heynemann¹¹ which were published in 1913.

Heynemann's observations were based on a study of 42 women during the last trimester of pregnancy of whom 37 were also examined after delivery. In addition 35 nonpregnant women were examined. The examination included a thorough physical examination, fluoroscopic examination, and teleoroentgenograms or orthodiagrams. In 10 women both teleoroentgenograms and orthodiagrams were made. The teleoroentgenograms were made on quiet respiration with the subject standing, the tube being centered to the left of the spinal column at the height of the cardiac apex at a distance of 2 to 2.5 meters. Orthodiagrams were made with the subject sitting, the position of the heart and diaphragm on forced inspiration and on forced expiration being determined. From these studies Heynemann found that without exception there was an elevation of the diaphragm toward the end of pregnancy. The degree was highly variable being from 0.25 to 4 cm. The average was 2.11 cm. During quiet respiration there was no definitely recognizable difference between the pregnant and nonpregnant states. During forced respiration Heynemann found that on deepest inspiration the diaphragm cannot descend as deeply in the pregnant as in

the rectum, while the tip of the other arm is brought up externally against the sacrum at the point marked.

The length of the posterior sagittal diameter of the midplane is now determined by subtracting from the first measurement the reading obtained for the thickness of the sacrum, and the value previously obtained for the length of the anterior sagittal diameter of the narrow pelvic plane.

A posterior sagittal diameter of the midplane of 5.5 cm. or less may usually be regarded as an android character.

THE COMPARATIVE EFFECTS OF PREGNANCY AND PHRENIC NERVE INTERRUPTION ON THE DIAPHRAGM AND THEIR RELATION TO PULMONARY TUBERCULOSIS

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AS LONG as women have tuberculosis, the medical profession will be faced with the problem of tuberculosis and pregnancy. At the present time there is no unanimity of opinion as to how a pregnant woman with tuberculosis should be treated. Notwithstanding the multitudinous opinions on this subject, there are insufficient scientific data upon which to base a sound conclusion. In this paper we do not wish to discuss the problem as a whole, but wish merely to direct attention to one phase of it. *This study is concerned with the hypothesis that the pregnant uterus has an effect upon the diaphragm similar to that produced by section of the phrenic nerve, namely elevation and paralysis of the diaphragm.*

In attempting to trace the development of the present ideas concerning the action of the diaphragm in pregnancy, we searched 120 obstetric textbooks of separate titles supplemented by 50 later editions.

The first reference to the diaphragm was found in the 1831 translation by Meigs of Velpeau's work.¹ It states: "The diaphragm itself being pushed upward into the thorax, whose base it enlarges, while its vertical diameter is lessened, is in some degree hindered from executing its contractile movement." In 1866 Dohrn found that in most cases the base of the thorax during pregnancy has a greater transverse but smaller anteroposterior diameter, thus partially compensating for the decreased vertical diameter. In succeeding works, these two ideas have been continued in part or in whole. By 1907² the addition of a third idea had appeared, namely, that during pregnancy the breathing is more thoracic than abdominal in type. The latest works available³⁻⁶ continue the same ideas. For instance, DeLee⁷ states: "The respiration is more costal than abdominal because of the restricted excursion of the diaphragm; yet the lung capacity is increased, breathing deeper and more frequently—cause, acidosis?"

In this case we assume that preoperative corresponds to postpartum, both representing the normal state, and that postoperative corresponds to antepartum. In this case the ninth thoracic vertebra is used as the point of comparison. First considering the level of the diaphragm on expiration (solid line, Fig. 3), we see that there is no marked difference between the preoperative and postoperative levels, nor is the diaphragm level affected much by a change from the vertical to the horizontal

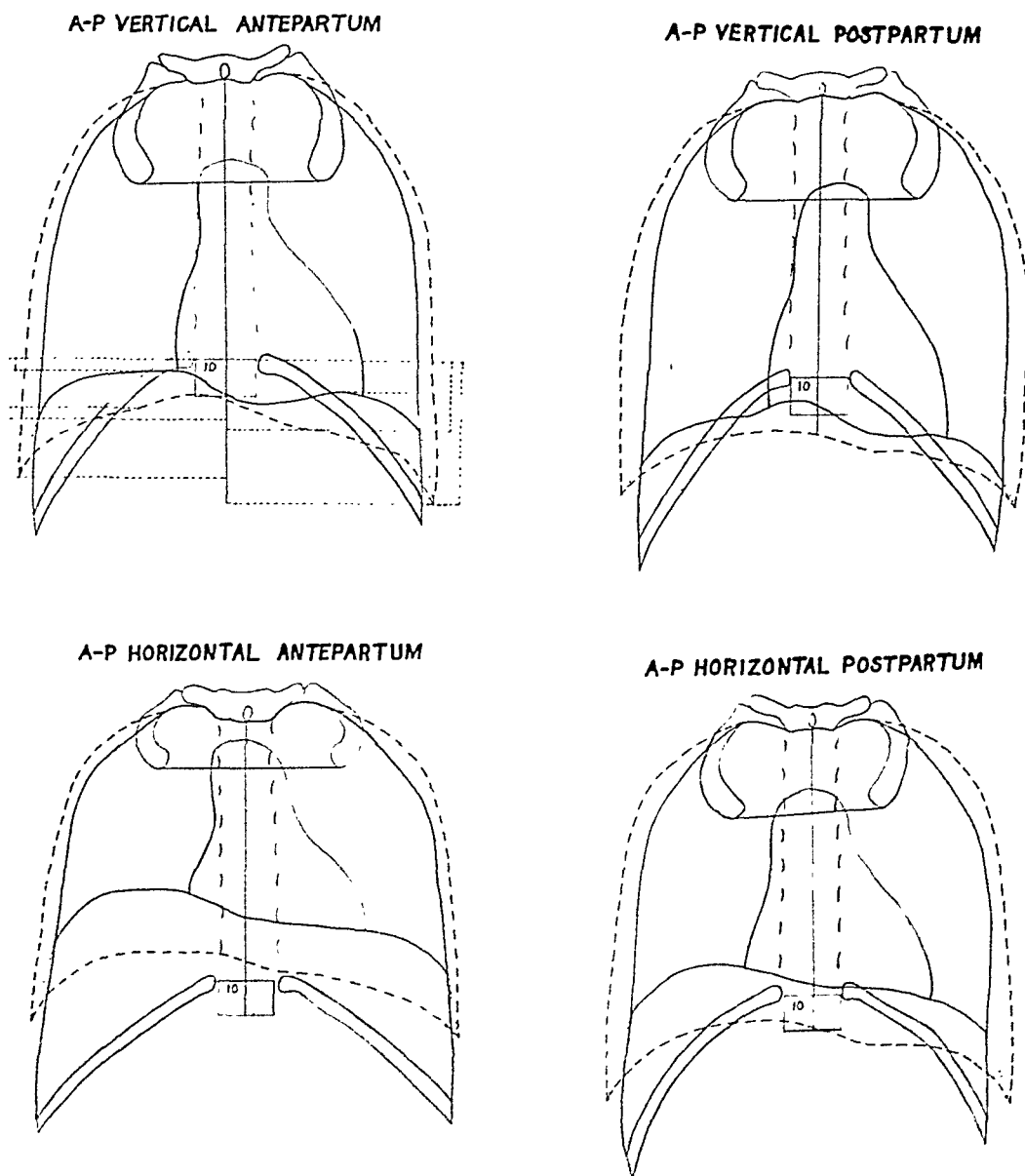


Fig. 1.—Lung outlines traced from anteroposterior teleoroentgenograms of dolichomorphic I. K. The solid line indicates their position on forced expiration; the broken line on forced inspiration. The dotted lines between the costophrenic sinuses on inspiration and expiration complete the delineation of the area of diaphragmatic excursion. In the upper left hand outline, the horizontal lines are reproduced to show the means by which the measurements were obtained for Tables III and IV.

position. This is a decided contrast to the response to pregnancy shown by dolichomorphic I. K. in Fig. 1. Next considering the right diaphragm on forced inspiration (broken line), we see that in the vertical position there is no marked difference between the preoperative and postoperative states. In the horizontal position, the diaphragmatic excursion on the right is somewhat greater postoperatively

the nonpregnant woman, but on complete expiration it rises so much higher that he "was forced to the unqualified conclusion that the excursion of the diaphragm even at the end of pregnancy is not at all or only very remarkably little impaired."

To show the difference between the effect of phrenic nerve interruption and pregnancy on the action of the diaphragm, we decided to determine the position of the diaphragm, the extent of its movement, and the direction of its movement in subjects during pregnancy and after delivery and in a subject before and after phrenic palsy. Our studies were made with the use of the teleoroentgenogram at 72 inches. The subject maintained forced inspiration while an exposure was made; she then exhaled into a spirometer and maintained the forced expiration until the second exposure had been made on the same film. Such composite negatives were made with the subject in the anteroposterior, the right posterior oblique, and the left posterior oblique projections both vertical (standing) and horizontal (lying). In the right lateral projection it was necessary to use separate films for inspiration and expiration. The tube was centered at the level of the xiphoid.

On the films thus obtained the lung borders were outlined with a wax pencil. These outlines and certain skeletal landmarks were traced on paper and from these tracings our measurements were obtained. The tracings for dolichomorphic I.K. are shown in Figs. 1 and 2. The lung borders on forced expiration are shown by a solid line; on forced inspiration the lung borders are shown by a broken line. Using the tenth thoracic vertebra as a point of comparison, and comparing the left hand outlines with the right hand ones, we see that the diaphragm level is higher antepartum than postpartum. When we compare the upper and lower outlines we see that the diaphragm is higher when the subject is lying (horizontal) than when she is standing (vertical). Comparison of the diaphragmatic excursion reveals that it is greater antepartum than postpartum and greater horizontal than vertical.

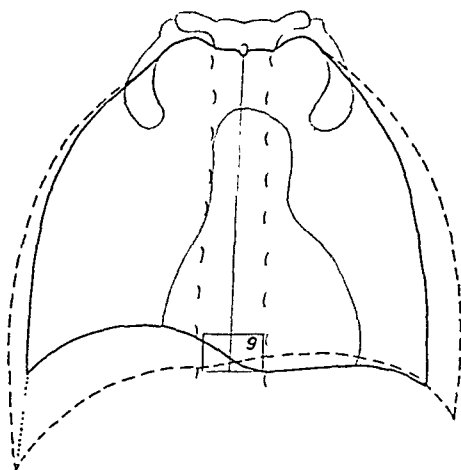
Figs. 1 and 2 were taken from the following case: I. K. (No. 267487), a healthy white female, aged fifteen years, height 163 cm., antepartum weight 57.5 kilograms, was of a dolichomorphic habitus. The antepartum studies were obtained sixteen days before the normal spontaneous delivery of a 4,260 gm. healthy infant. The postpartum studies were made on the eleventh day of the puerperium. This subject is referred to as "dolichomorphic I. K." in Tables I, II, III, and IV. Her lung outlines are portrayed in Figs. 1 and 2.

The above case of a pregnant woman is to be compared with the following case of a woman with left phrenic nerve interruption: H. W. (No. 285596), a white female, aged thirty years, height 157 cm., weight 49.5 kilograms, was of an intermediate habitus. She had minimal pulmonary tuberculosis at the left apex. Studies were obtained the day before a left temporary phrenic nerve interruption was performed and again on the thirteenth postoperative day. This subject is referred to as "H. W. (Left Phrenic)" in Tables I, II, III and IV. Her lung outlines are portrayed in Fig. 3.

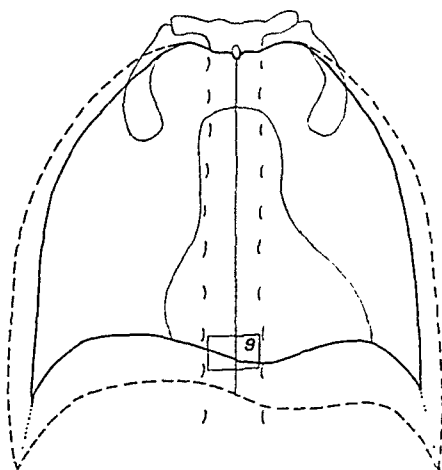
of the diaphragm on both sides on inspiration and on expiration was measured in millimeters. If there was not a definite dome, a point on the diaphragm perpendicular to the tip of the first rib was used. (See Fig. 1, left upper outline.)

With the aid of a planimeter, the area within the lung borders was determined in square centimeters. No attempt was made to subtract the contents of the mediastinum as these remain relatively constant. The area of excursion of the

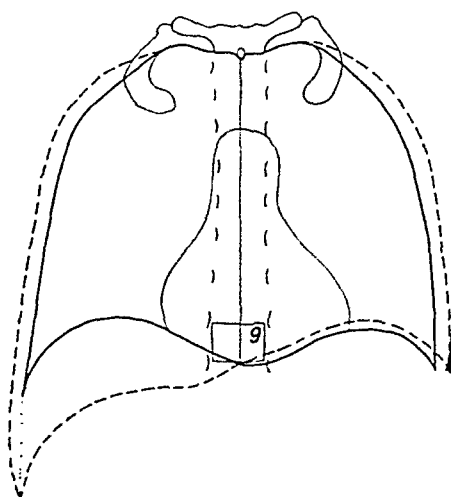
A-P VERTICAL POSTOP.



A-P VERTICAL PREOP.



A-P HORIZONTAL POSTOP.



A-P HORIZONTAL PREOP.

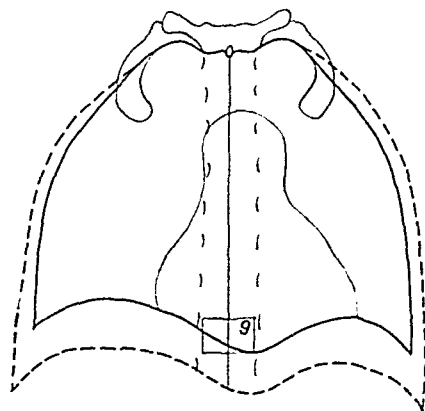
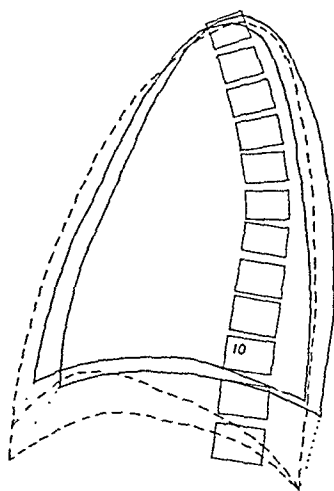


Fig. 3.—Lung outlines traced from anteroposterior teleoroentgenograms of H. W. (left phrenic). Solid line represents expiration; broken line inspiration.

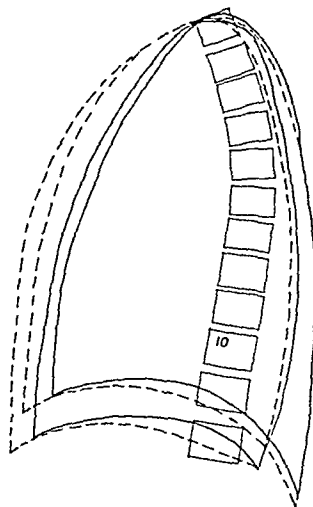
lung as projected was determined by subtracting the expiratory area from the inspiratory area. The diaphragmatic excursion was determined as the area outlined by the level of the diaphragm on inspiration and on expiration supplemented by a (dotted) line drawn on either side between the costophrenic sinus in the two phases of respiration. The proportion of respiration accomplished by the excursion of the diaphragm was expressed as a percentage by dividing the area of diaphragmatic excursion by the area of the total excursion of the lung (Table I).

than preoperatively. However, on the left side we find a marked difference in the presence of the left phrenic palsy. On inspiration, instead of descending as it did normally preoperatively, the left diaphragm rises. This action of the paralyzed diaphragm is known as paradoxical motion. Although it is shown to some extent in the outlines in Fig. 3, paradoxical motion can be seen to much greater advantage under the fluoroscope. It is brought out best by having the patient make a sudden inspiration in the nature of a "sniff." The paralyzed diaphragm then rises sharply

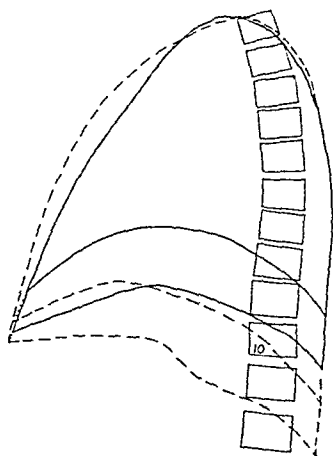
R.LAT. VERT. ANTEPARTUM



R.LAT. VERT. POSTPARTUM



R.LAT. HORIZ. ANTEPARTUM



R.LAT. HORIZ. POSTPARTUM

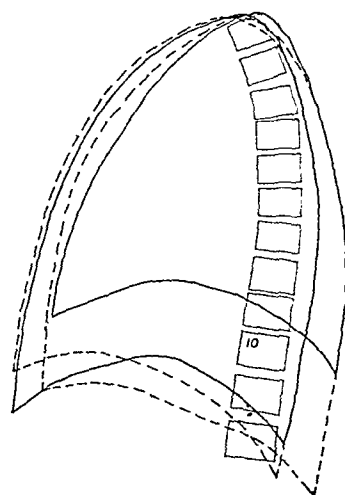


Fig. 2.—Lung outlines traced from right lateral teleoroentgenograms of dolichomorphic I. K. Solid line represents expiration; broken line inspiration.

for a fraction of a second before falling back to a less extreme position as shown in Fig. 3. In addition to the paradoxical motion of the left diaphragm postoperatively, it is seen that its excursion is much less than it was preoperatively.

In order to confirm mathematically the impressions gained from a study of Figs. 1, 2 and 3, measurements were made in following manner: In the A-P projection, a horizontal line was drawn across the upper border of the vertebra outlined, and from this line the perpendicular distance to the costophrenic sinus and to the dome

Table II, showing the comparison of the diaphragmatic excursion percentage values antepartum and postpartum, was composed from the values given in Table I. In this comparison it is seen that in the case of dolichomorphic I. K. the diaphragmatic excursion percentage is greater antepartum than postpartum both vertically (30 per cent) and horizontally (7 per cent). In the case of brachymorphic E.C.,* the percentage is greater antepartum than postpartum vertically (10 per cent) but less horizontally (-8 per cent). However, the average of the percentages in the two positions reveals an insignificantly greater value for the antepartum state (1 per cent). In the case of H. W. (left phrenic) we again assume that postoperative corresponds to antepartum, and preoperative to postpartum. In the comparison in Table II we see that the diaphragmatic excursion percentage is less postoperative than preoperative both vertically (-16 per cent) and horizontally (-39 per cent). Thus we find that the percentage in a case of left phrenic palsy is diametrically opposed to the percentage in cases of pregnancy.

TABLE II. DIAPHRAGMATIC EXCURSION PERCENTAGE GREATER ANTEPARTUM THAN POSTPARTUM*

	DOLICHOMORPHIC I. K.			BRACHYMORPHIC E. C.			H. W. (LEFT PIIRENIC)		
	RIGHT PER CENT	LEFT PER CENT	SUM PER CENT	RIGHT PER CENT	LEFT PER CENT	SUM PER CENT	RIGHT PER CENT	LEFT PER CENT	SUM PER CENT
A.-P. Vertical	15	18	17	12	5	9	13	-80	-19
R. Lat. Vertical	39	46	43	11	9	10	7	-61	-13
Aver. Vertical			30			10			-16
A.-P. Horizont.	17	13	15	6	-2	2	-3	-117	-18
R. Lat. Horizont.	-19	31	-1	-13	-24	-18	-115	-54	-60
Aver. Horizont.			7			-8			-39
Total Average			19			1			-28

*Diaphragmatic excursion percentage (D/Dif. in Table I) greater antepartum than postpartum for dolichomorphic I. K. and brachymorphic E. C. Under H. W. (left phrenic), the comparison is postoperative greater than preoperative. Negative values indicate the diaphragmatic excursion percentage is greater postpartum than antepartum or greater preoperative than postoperative.

It is interesting to note that in the case of dolichomorphic I. K. the diaphragmatic excursion percentage averages 68 per cent antepartum and 49 per cent postpartum. In the case of brachymorphic E.C. the averages are 70 per cent antepartum and 69 per cent postpartum. H. W. (left phrenic) represents averages of 55 per cent postoperative and 83 per cent preoperative. Thus we find in the planimeter values from our two cases studied antepartum and postpartum that contrary to the general belief the diaphragmatic excursion is greater antepartum than postpartum and that respiration antepartum is more diaphragmatic than costal.

Next we consider the excursion of the costophrenic sinuses and domes of the diaphragm as shown in Table III. In the case of dolichomorphic I. K. we see that the excursion of the costophrenic sinuses in the vertical position is much greater antepartum than postpartum. In the horizontal position, the excursion is greater postpartum than antepartum. However, the excursion of the domes of the diaphragm is greater antepartum than postpartum both vertically and horizontally. The values in the case of brachymorphic E.C. show a greater excursion postpartum

*E. C. (#369887), a healthy white female, aged seventeen years six months, height 155 cm., antepartum weight 66.4 kilograms, was of a brachymorphic habitus. The antepartum studies were obtained twenty-two days before the normal spontaneous delivery of a 3,400 gm. healthy male infant. The postpartum studies were made on the tenth day of the puerperium. This subject is referred to as "brachymorphic E. C." in Tables I, II, III, and IV. The lung outlines from which the data in the tables was obtained are not reproduced for this case as they differed in no essential respect from those shown for 'dolichomorphic I. K.'

TABLE I*

PLANIMETER READINGS IN SQUARE CENTIMETERS

	SPR. C.G.	RIGHT				LEFT				SUM OF R. & L.							
		INSP.	EXP.	DIF.	DIA.	D/DIF.	INSP.	EXP.	DIF.	DIA.	D/DIF.	INSP.	EXP.	DIF.	DIA.	D/DIF.	
<i>Dolichomorphia I.K.</i>																	
A-P. Vert. Antepartum	----	228	178	50	27	54%	267	214	53	27	51%	392	103	54	52%		
A-P. Vert. Post.	1700	237	193	44	17	39%	280	231	49	16	33%	424	93	33	35%		
A-P. Horiz. Ante.	1790	183	124	59	47	80%	213	150	63	43	68%	274	122	90	74%		
A-P. Horiz. Post.	1790	230	159	71	45	63%	243	176	67	37	55%	335	138	82	59%		
R. Lat. Vert. Ante.	----	319	252	67	39	58%	348	272	76	54	71%	667	143	93	65%		
R. Lat. Vert. Post.	1810	340	287	53	10	19%	348	304	44	11	25%	688	591	21	22%		
R. Lat. Horiz. Ante.	----	271	178	93	73	78%	334	249	85	69	81%	605	427	178	80%		
R. Lat. Horiz. Post.	----	330	225	105	102	97%	374	322	52	26	50%	704	547	157	81%		
<i>Brachymorphia E.C.</i>																	
A-P. Vert. Ante.	----	226	180	46	32	70%	240	194	46	33	72%	466	374	92	65	71%	
A-P. Vert. Post.	2320	249	175	74	43	58%	263	194	69	46	67%	512	369	143	89	62%	
A-P. Horiz. Ante.	2250	191	129	62	43	69%	197	141	56	33	59%	388	270	118	76	64%	
A-P. Horiz. Post.	2360	248	149	98	62	63%	231	154	77	47	61%	479	303	175	109	62%	
R. Lat. Vert. Ante.	2280	357	255	102	72	71%	391	286	105	79	75%	748	541	207	151	73%	
R. Lat. Vert. Post.	2300	385	274	111	67	60%	385	281	104	69	66%	770	555	215	136	63%	
R. Lat. Horiz. Ante.	----	325	220	105	77	73%	367	259	108	78	72%	692	479	213	155	72%	
R. Lat. Horiz. Post.	----	348	229	119	102	86%	410	326	84	81	96%	758	555	203	183	90%	
<i>II. IV. (Left Phrenic)</i>																	
A-P. Vert. Postop.	1900	209	161	48	35	73%	193	168	25	-5	-20%	402	329	73	30	41%	
A-P. Vert. Preop.	1800	222	167	55	33	60%	217	159	58	35	60%	439	326	113	68	60%	
A-P. Horiz. Postop.	1250	235	164	71	48	68%	178	166	12	-6	-50%	413	330	83	42	51%	
A-P. Horiz. Preop.	1000	185	143	42	30	71%	196	151	45	30	67%	381	294	87	60	69%	
R. Lat. Vert. Postop.	1640	332	191	141	89	63%	308	261	47	2	4%	640	452	188	91	48%	
R. Lat. Vert. Preop.	1550	322	211	111	62	56%	368	243	125	81	65%	690	454	236	143	61%	
R. Lat. Horiz. Postop.	----	329	216	113	96	85%	275	266	9	3	33%	604	482	122	99	81%	
R. Lat. Horiz. Preop.	----	344	330	14	28	200%	362	347	15	13	87%	706	677	29	41	141%	

*Planimeter readings in square centimeters from teleoroentgenograms taken in circumstances designated in left-hand column. The second column (Spr.) gives the spirometric reading in cubic centimeters obtained between the taking of the inspiration (Insp.) and expiration films. The next five columns show in order: The internal area of the thorax to the right of the midline on inspiration (Insp.); on expiration (Exp.); the area of excursion of the right lung (Dif.) as given by the difference between the area of inspiration (Insp.) and expiration (Exp.); the excursion of the right diaphragm (Dia.); the ratio of diaphragmatic to total respiration (D/Dif.) obtained by dividing the former (Dia.) by the latter (Dif.). The next five columns show the corresponding values for the left side. The last five columns show the sum of the values for the right and left sides.

rotation of the subject is most strikingly brought out in the case of H.W. (left phrenic) in the right lateral horizontal preoperative projection (Table I). The inspiratory projection is practically a true lateral but the expiratory film shows some rotation, thus increasing the projection of the A-P diameter and the total area so that it approaches the inspiratory value. The diaphragmatic levels are not proportionately affected by the rotation. As a result the excursion of the right diaphragm as projected is greater than the total excursion recorded for the right side.

In our determinations we have assumed that the postpartum values obtained on the tenth and eleventh days of the puerperium represent the normal nonpregnant state.

This assumption is based on the work of Alward¹² who made daily vital capacity determinations on 60 pregnant women during the last month of pregnancy and during the puerperium. The patients were allowed up on the tenth day and discharged on the fourteenth day of the puerperium. Final determinations were made on the postpartum visit one month to six weeks after delivery. As a result of these observations Alward concluded that "in the majority of cases there is normally a gradual reduction in the vital capacity in the last month of pregnancy. This is especially noticeable during the two-week period before delivery. Following delivery there is a fairly sharp reduction in the vital capacity with a gradual return to normal limits which is reached by the tenth day of the puerperium and remains so throughout the following days of the puerperium."

The spirometric readings obtained between the inspiratory and expiratory exposures varied (Table I). This introduces another source of error. From our data we are unable to say what effect a variation in the spirometric reading has upon the ratio of the diaphragmatic to the total respiratory excursion. In comparing the antepartum and postpartum determinations in our two subjects we find that the several antepartum readings average 1923 c.c.; the postpartum readings average 1943 c.c.

We realize that the data from two cases of pregnancy, especially with the unrefined methods described, would be insignificant if used alone. Therefore we wish to call attention to the work of Klawns and Palugay,¹³ who have performed an extensive investigation.

In fifty women, during the last weeks of pregnancy and up to the tenth postpartum day, they made orthodiagraphic tracings with the subjects standing and lying, during forced inspiration and expiration and quiet inspiration and expiration. From these tracings they obtained vertical measurements from a horizontal line drawn through the midclavicular points to the costophrenic angle and to the dome of the diaphragm on the right and on the left in the four phases of respiration. The measurements thus obtained in the fifty women were averaged. The average values given in the body of the paper by Klawns and Palugay have been assembled and are presented in Tables III and IV under K. and P. (Aver. 50 cases).

than antepartum of the costophrenic sinuses and domes of the diaphragm both vertically and horizontally. In considering the values for H.W. (left phrenic), still assuming that postoperative and antepartum are the comparable states, we find a marked variation from the above two cases. The functioning right diaphragm has a greater excursion postoperatively than preoperatively, but the dome of the paralyzed left diaphragm reveals its paradoxical motion postoperatively by the negative values.

TABLE III. DIAPHRAGMATIC EXCURSION IN MM.*

	COSTOPHRENIC SINUS				DOME OF DIAPHRAGM			
	RIGHT		LEFT		RIGHT		LEFT	
	ANTE.	POST.	ANTE.	POST.	ANTE.	POST.	ANTE.	POST.
<i>Dolichomorphic I. K.</i>								
Forced Resp. Vert.	37	18	49	17	23	12	25	9
Forced Resp. Horiz.	49	58	47	48	40	38	34	34
<i>Brachymorphic E. C.</i>								
Forced Resp. Vert.	38	66	40	55	23	31	24	37
Forced Resp. Horiz.	54	101	40	63	41	48	33	45
<i>H. W. (Left Phrenic)</i>								
Forced Resp. Vert.	57	37	20	48	31	26	-6	36
Forced Resp. Horiz.	57	38	0	34	41	29	-3	27
<i>K. & B. (Aver. 50 Cases)¹³</i>								
Forced Resp. Vert.	37	37	49	34	39	18	52	23
Forced Resp. Horiz.	69	65	63	61	51	49	53	47
Quiet Resp. Vert.	13	12	13	13	9	8	11	10
Quiet Resp. Horiz.	13	15	12	11	11	11	11	10

*Excursion of diaphragm in millimeters between forced inspiration and expiration measured at the costophrenic sinus and at the dome of the diaphragm on the right and on the left with the subject standing (Vert.) and lying (Horiz.). For dolichomorphic I.K., brachymorphic E. C. and K. and P. (Aver. 50 cases)¹³ values for the antepartum (Ante.) and postpartum (Post.) states are given in adjacent columns. For H. W. (left phrenic) postoperative values are given in columns headed Ante. and preoperative values in columns headed Post.

The figures obtained in the above described manner are not to be taken as absolute values. They are of significance only as a basis for relative comparisons. There are many sources of error. The projection of the diaphragm varies if the x-ray tube is not centered at the same level. In outlining the position of the diaphragm within the cardiac shadow it is necessary to be somewhat dogmatic. A true anteroposterior projection can usually be obtained, but this projection gives us information regarding the position of the diaphragm in one plane only. For this reason we made teleorentgenograms with the subjects in the additional projections. It is in these additional projections that the source of error is greatest. In the oblique projections it was impossible to obtain films with the subject in the same degree of rotation, antepartum and postpartum, or vertical and horizontal. Also the delineation of the diaphragm shadow on the oblique projections was uncertain. These difficulties made the determinations for the oblique projections so variable and uncertain that the results were discarded. We also found it difficult to get a true lateral projection. The error caused by a slight

In Table IV we see that the diaphragm is higher antepartum than postpartum, being much more so on forced expiration than on forced inspiration. Under K. and P. (aver. 50 cases) the value for forced inspiration at the left dome of the diaphragm is -17 mm. This is surprising for it means that the left dome of the diaphragm on forced inspiration in the vertical position is lower antepartum than postpartum in spite of the gravid uterus.

SUMMARY

One of the arguments frequently given for the conservation of pregnancy in a tuberculous patient is that the gravid uterus elevates the diaphragm and acts as a splint, thus giving the effect of a phrenic nerve interruption. However, the work of Heynemann, the work of Klafien and Palugyay, and our observations show that the diaphragm on expiration is higher antepartum than postpartum, but on inspiration the diaphragm descends to a level that is more nearly comparable to that of the puerperal state. Therefore, in pregnancy, the diaphragm, instead of being splinted, tends to have a greater excursion on forced respiration than in the nonpregnant state. In contradistinction to this the paralyzed diaphragm ascends on inspiration, and it is only this paralyzed diaphragm that has been shown to be of value in pulmonary tuberculosis. The actively functioning diaphragm, though high in position, has never been demonstrated to be of value in pulmonary tuberculosis. Therefore, the hypothesis that tuberculosis may be benefited by the effect of pregnancy on the diaphragm is not justified.

The author wishes to express his appreciation for the courtesy and assistance extended to him by Dr. John B. Barnwell and Dr. Carleton B. Peirce.

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The respiratory movements of the diaphragm were without exception greater antepartum than postpartum as indicated in Table III. On an average, the excursion was greater on the left than on the right (average 48 mm. and 46 mm., respectively), and greater in the costophrenic sinuses than in the region of the domes (average 52 mm. and 42 mm.). The values for quiet respiration in Table III are in accord with Heynemann's statement that there is no essential difference in quiet respiration between the pregnant and puerperal states.

Although values for individual cases are not given, these authors state that the ratio of diaphragmatic and thoracic respiration depends on the constitutional type. The diaphragmatic excursion antepartum and postpartum, and both horizontal (lying) and vertical (standing), was more marked in dolichomorphic than in brachymorphic women. This observation, that the diaphragmatic excursion is greater in dolichomorphic women, is of added interest when we correlate it with the observation that a majority of tuberculous patients are of an asthenic habitus.

The difference between the diaphragmatic excursion antepartum and postpartum was more marked in the standing than in the lying position. However, both antepartum and postpartum the excursion of the diaphragm during forced respiration was greater when the subject was horizontal than when vertical. This is of significance, for rest in bed (horizontal position) is the basis for treatment of pulmonary tuberculosis.

TABLE IV. HIGHER POSITION OF DIAPHRAGM ANTEPARTUM THAN POSTPARTUM IN MM.*

	VERTICAL				HORIZONTAL			
	SINUS		DOME		SINUS		DOME	
	RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT
<i>Dolichomorphic I.K.</i>								
Forced expiration	21	22	19	18	36	28	40	34
Forced inspiration	2	-10	8	2	45	29	38	34
<i>Brachymorphic E.C.</i>								
Forced expiration	14	11	15	9	24	27	28	22
Forced inspiration	42	26	23	22	71	50	35	34
<i>H.W. (Left Phrenic)</i>								
Forced expiration	13	10	4	-10	-43	-5	-11	-3
Forced inspiration	-7	38	-1	32	-62	29	-23	27
<i>K. & P. (Aver. 50 Cases)¹³</i>								
Forced expiration	29	18	16	14	21	16	16	12
Forced inspiration	29	3	5	-17	16	14	14	6
Quiet expiration	28	15	16	11	24	19	18	14
Quiet inspiration	27	15	15	10	26	18	18	13

*Higher position of diaphragm antepartum than postpartum in millimeters at the costophrenic sinus and dome on the right and on the left. For H. W. (left phrenic) the comparison is higher postoperative than preoperative. Negative values indicate higher postpartum than antepartum or higher preoperative than postoperative.

6 dr. or more, and within approximately twenty hours of its administration the antiproteolytic factor related to the onset of abortion disappeared from the blood serum. This factor was later proved to be an estrogenic substance.^{9, 10} Its disappearance from the serum coincided with subsidence of the symptoms and signs of abortion. If none but the initial dose were given the antiproteolytic estrogenic factor reappeared in the serum on the average in four days or a little more, and simultaneously symptoms and signs of impending interruption of pregnancy might or might not recur promptly. It therefore became our routine to administer within the first twenty-four hours of therapy three doses, each of 4 dr., of wheat germ oil (roughly twice the minimal dose required), and to follow this with 1 dr. of oil each day.

It should be understood that the oil used was at first a fresh ether-extracted wheat germ oil, kept in a refrigerator until and during use. In the past year and a half a cold pressed oil has been used in its stead. Its dosage appears to be the same.

We have not undertaken any extended clinical or laboratory analysis of any of the other wheat germ oils now on the market. The oil used has been prepared by a standardized technique but has not been standardized pharmacologically. It was known to possess fairly consistently a satisfactory content of vitamin E. Not only has it remained effective in clinical cases, many of which are always under observation and are periodically checked for the reappearance of antiproteolysis in their serums, but it has been checked repeatedly on E-free rats during the past two years. The early workers with wheat germ oil have pointed out that some wheat germ seems to be quite defective in vitamin E content. The reason is as yet unknown.

Bacharach¹¹ has recently pointed out that it is very doubtful if there can be a standard preparation or a unit of vitamin E, for no biologic standardization is possible. It certainly does not seem to be commercially feasible to standardize a wheat germ oil of the type used by us. To do so would entail its administration to a group of E-free rats in such quantities and under such controlled conditions as would ensure a pregnancy carried to a successful conclusion. This would require twenty-one days on the average. For reasons to be given later it appears that the length of time during which wheat germ oil remains potent is little more than eight weeks even when kept under optimum conditions. There would, in short, be only five weeks during which animal-standardized samples of the oil could be distributed and sold. This would scarcely be practicable.

There has been accumulating recently a most interesting body of evidence to indicate that there are enormous variations in the capacities of different individuals to assimilate the various known vitamins.

WHEAT GERM OIL THERAPY

I. DOSAGE—IDIOSYNCRASY

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VERY little has appeared in the literature on the practical problems involved in wheat germ oil therapy. A rational basis for dosage, some indication of the variations in dose demanded by different types of cases, what dosage if any is excessive, whether idiosyncrasies occur, all of these points require elaboration. How long will wheat germ oil retain its potency unchanged and what are the optimal conditions for its preservation? What is its effect upon the onset and duration of normal labor if it is administered until labor begins at term? Are there pathologic processes other than habitual abortion in which it is of value, and where failures occur, to what should they be ascribed? These problems are examples of those that remain to be studied.

It is in the hope of throwing some light into these corners that the following analysis of clinical experiences with a group of 115 female and 12 male patients is presented. A dozen or so of these have been already included in the Watson and Tew report¹ on the influence of wheat germ oil therapy on abortion.

DOSAGE

There seems to be no general agreement about the dosage of wheat germ oil required by patients of various clinical types.

Early in the experimental work on the subject, Evans and his coworkers² determined the minimal single dose of the oil which would protect an E-free rat from resorbing or aborting its young. Various other authorities, Juhasz-Schaffer,³ Sure,⁴ and Gierhake⁵ have similarly estimated this rat dose using various oils and concentrates. However, such estimates have relatively little value in deciding upon the dosage to be administered to human patients. The first workers⁶ in the clinical field in most cases used 2 to 3 gm. as the daily dose from the time treatment was begun. No precautions as to storage or the variations in individual requirement were urged in their reports. So far as we can discover, there has never been any precise indication for quantitative dosage given except that mentioned in an earlier publication of ours.⁷

We stated that sufficient wheat germ oil should be given to render the blood serum of the patient under consideration normally digestible by a dilute trypsin solution under the precise conditions of the test we had elaborated.⁸ It was found that many women threatening to abort would not do so if given a single massive dose of the oil, supplemented by smaller daily doses thereafter. The usual initial dose required was

dividual that we have proposed.⁷ Neglect to observe the variations in the requirement of wheat germ oil probably explains many or most of the "failures" occurring in patients under treatment with it. So frequently, when our study was in its early stages, did we find patients continuing to bleed and threatening to abort or miscarry on the continuing dosage of one dram per day that we came to rely upon our serologic test for the control of the patient. Otherwise the first indication of an inadequate continuing dose would occasionally present itself in the form of ruptured membranes. The most appropriate index for treatment at the moment appears to be the disappearance of the antiproteolytic estrogenic factor from the blood serum.

When large doses were first employed, there was some anxiety lest they prove toxic. However, both Juhasz-Schaffer and Evans and Burr had established the fact that no bad effects could be discerned in rats given much larger doses than they usually required. Our clinical experience has amply demonstrated the safety of large doses. We have treated many women with 4 to 6 dr. of wheat germ oil each day for months, and one woman took three ounces each day for two months. In no case was any untoward effect observed. Watson and Tew¹ have also stated that doses as high as 20 c.c. per day were not observed to have any harmful influence. It should be pointed out, however, that the great majority of women are adequately controlled by the usual initial dose of 6 to 12 dr., followed by 1 dr. each day.

It is worthy of comment that in almost every instance in which an unusually large dose of wheat germ oil has been required for the preservation of pregnancy, the patient has been a case of hypothyroidism. It may be, of course, that this study was conducted in an area in which a very large proportion of such cases was present—indeed, we have felt that such was the case. Whatever the explanation is, the fact has been very impressive. These hypothyroid women appear either to manufacture great excesses of the estrogenic antiproteolytic factor or to be unable to excrete it adequately. That the latter may prove to be the correct alternative is suggested by the animal work of Van Horn,²⁰ and of Weichert and Boyd.²¹ Benazzi²² also illustrated the relationship between estrin and the thyroid gland by injecting rats with estrin and producing marked thyroid hypoplasia.

Up to the present we have found 39 individuals who required a maintenance dose of the oil of at least triple the usual daily 1 dr.; of these three had basal metabolic rates before pregnancy of between 13 and 20 per cent below normal. None of the remaining 36 had had basal metabolic rates taken, but 25 of the 36 had had definite symptoms and signs of hypothyroidism such as antegestational menorrhagia, poor cold tolerance, great fatigability, constipation, and dry skin. These symptoms were promptly controlled by doses of thyroid extract and recurred in whole or in part when the thyroid extract was discontinued. Indeed

Moncrieff¹² reported the development of scurvy in a child receiving a diet adequate in vitamin C and rickets appearing similarly on a diet adequate in vitamin D. Thatcher,¹³ on the contrary, reported fatal hypervitaminosis D occurring on a dietary containing a not unusually large intake of cod liver oil. Ayad¹⁴ cited the case of a man unharmed by a prodigious intake of cod liver oil over a period of six years, and several other cases unharmed by huge doses of vitamin D over a considerable period of time. Moreover, as regards vitamin B₁, Baker and Wright¹⁵ have indicated that beriberi may develop on a diet containing anything from 71 to 382 international units (indeed that it occurs in Ireland on a diet containing 438 units), that there is a distinct difference in the minimal requirement of Europeans and natives in the Dutch East Indies, and that during pregnancy, in experimental animals at least, the requirement rises three to five times. Jeans and Zentmire¹⁶ working with vitamin A and Gothlin and his coworkers¹⁷ with vitamin C have demonstrated that a large proportion of the population of various countries exists in a chronic state of hypovitaminosis hitherto unsuspected.

It would seem, therefore, that contrary to the opinion of Sure¹⁸ and some other authorities, we might suspect the existence of a state of hypovitaminosis in respect to vitamin E in people living apparently normally on the mixed dietary of Canada and the United States. As Vogt-Miller¹⁹ also has observed, similar rats identically fed become E-defective on a diet deficient in vitamin E after varying intervals of time.⁷ He early pointed out that women in Denmark on ordinary diets could not be suspected a priori of E deficiency. Yet he admitted that a few women might require more of this vitamin than did the average. Similarly we have found large differences in the amount of wheat germ oil required to nullify the effects of E-deficiency in the human being. The largest daily dosage required to date has been twenty-four drams of wheat germ oil a day. A point we should like to stress is that if the patient requiring a large dose received anything short of that dose, she derived very little benefit from it. She went on to display most of the symptoms which would show themselves had no treatment been instituted. As we understand it, the major requirement of such therapy is that it should be sufficient to remove the estrogenic antiproteolytic factor from her blood serum, as evidenced by the author's test, and hold it in abeyance.

When one considers the large number of wheat germ oils now on the market, the question of "quality versus quantity" in matters of dosage must arise. There appears to be a different requirement in each case, depending on the varying concentration of the antiproteolytic estrogenic factor in the blood and the amount of vitamin E actually present in any wheat germ oil preparation used. Since these factors are so variable, we feel that there is need of a standard of saturation, by which one may know when the particular patient under consideration at the particular stage of pregnancy she has reached at the moment, is brought under control with the particular kind and batch of wheat germ oil used. Quality is more important than quantity, obviously, and determines the latter. Hence the significance of the criterion of dosage for each in-

and excessive perspiration when first seen. Although extremely ruddy, her hemoglobin was only 57 per cent Sahli. She early developed evidences of toxemia of the abruptio placentae type²³ and this was controlled by an adequate dosage of ether-extracted wheat germ oil. She continued to gain weight rather excessively but her blood pressure was kept within bounds by a dose of as much as 8 dr. each day. After two months she experienced severe hot flashes lasting about five minutes each time and these recurred many times each day. She suffered from an unusually hot summer in a pitiable way. Finally, three months after her oil therapy had been instituted, she developed a generalized, raised, blotchy, reddish, discrete rash which was at times very itchy. She was tested for sensitivity to wheat by skin testing. (Courtesy of my colleague, Dr. Gordon Calder.) The wheat injection promptly produced an area closely resembling one of the blotches of her rash. Accordingly, her wheat germ oil therapy was discontinued and she was given a concentrate of the same marketed by another company. Her rash promptly disappeared, but such a huge dosage was required to control her toxemia and the antiproteolytic factor in her blood that the expense of the treatment was prohibitive. She reverted to the bulk oil therapy, but used a cold-pressed rather than an ether-extracted oil. There was a very slight flare-up of the rash and pruritus but never enough to render her unwilling to continue the use of this preparation. She took it till term, then stopped, and her rash and pruritus ceased in three days.

The other two instances in adults were not so striking but were definite. One woman developed a rash and the other an urticaria. Both were intensely itchy. The infantile sensitivity was noticed in a baby whose mother required wheat germ oil to effect lactation. During the whole period of time when the mother was treated with the oil, a matter of two weeks, the infant had numerous yellow stools filled with minute bubbles and containing a moderate proportion of clear mucus. Within two days of the cessation of the oil, the infant's stools became normal and remained so. The mother took four drams of the oil once again, when the child was three months old. The following day the child had a return of the characteristic stool, which remained as it was for a day, then reverted to normal. When the mother was not taking the oil, the child, which is now over five months old, never had anything but a perfectly normal stool.

SUMMARY

1. The most suitable routine dosage of ether-extracted or cold-pressed wheat germ oils of the type with which we have worked proved to be 12 dr. inside of the first twenty-four hours of treatment, followed by at least 1 dr. each day. The dosage varied with individual requirement, the quality of the oil used, and the stage of pregnancy.

2. A state of hypovitaminosis E appears to be relatively common among the pregnant women of this country.

3. Enormous doses of wheat germ oil seem to produce no untoward symptoms.

4. Of 39 women requiring huge doses of wheat germ oil, 28 were hypothyroid cases.

5. Six instances of idiosyncrasy to wheat germ oil are recorded.

NOTE.—In view of the recent report by Rowntree and others (*Am. J. Cancer* 31: 359, 1937) on the sarcogenic properties of crude ether-extracted wheat germ oil in rats, it should be pointed out that our study of patients treated with wheat germ oil was begun nearly four years ago.

we were able in three patients to render the patient's blood serum free of this antiproteolytic factor by means of the administration of thyroid extract alone.

IDIOSYNCRASY

We have seen five adult patients and one infant who have evinced signs of sensitivity to wheat germ oil.

One patient was a case of chronic asthma and recurrent hay fever, very highly allergic to many plant and animal proteins. In the course of routine tests done some years before she had been found sensitive to wheat. On three occasions a massive dose of ether-extracted wheat germ oil controlled threatened abortions and a maintenance dose of 4 dr. of the oil was required each day for a fortnight. With each compulsory return to the medication she developed increasing flatulence with nausea and vomiting. A period of one month elapsed during which no oil was administered. When it was given again, the above-mentioned symptoms were more marked than ever and very distressing. It was found necessary to discontinue the wheat germ oil therapy for a time, at least, and use one of the concentrates on the market. This produced less flatulence but still there was a great deal of it. She experienced the same generalized cutaneous "pricking" sensation with the concentrate as with the oil, and remarked that she had experienced this curious cutaneous sensation after the ingestion of certain foods, such as onion, to which she is allergic also. She chose to return to the oil therapy but this time a cold-pressed oil was used. Three weeks later, generalized pruritus forced her to stop. Near the end of her pregnancy, albuminuria and a rising blood pressure compelled her to return to the cold-pressed oil therapy. At once her nausea and extreme abdominal distention returned, rendering her so constantly uncomfortable that again the oil was discontinued. Labor was induced satisfactorily.

Another patient seen recently was a woman aged sixty years whose menopause developed six years ago. For the past three years she had had intense vaginal pruritus and vaginitis. The vaginal mucosa was raw, red, and acutely tender. No complicating parasitic infection nor glycosuria could be discovered. As a blood test revealed an excess of the estrogenic antiproteolytic factor she was given thyroid extract in the hope that it would remove the estrogenic substance from the blood. However, she proved intolerant of such therapy, for it produced tachycardia, palpitation, sweats, and insomnia. Then she was given ether-extracted wheat germ oil in the usual massive dose and carried along on 2 dr. each day. All her pruritus soon ceased and the raw red vaginitis disappeared in about four days. She remained improved for about two months, except for a monthly exacerbation of her pruritus for a period of approximately five days on each occasion. At the end of that time she had a bout of influenza and stopped taking her wheat germ oil while taking a good deal of other medication. When she returned to it, she experienced a sensation of intense "waves of heat" spreading all over her body and promptly displayed a generalized urticarial skin eruption. This was ascribed to strawberries, although that fruit had never affected her similarly before. She stopped her wheat germ oil therapy and promptly lost her sensations of heat and her rash; returning to treatment with cold-pressed wheat germ oil at once brought back her two complaints of heat and urticaria. At present she is unable to continue the use of wheat germ oil and her vaginitis is as troublesome as ever. We attempted to have this patient tested for sensitivity to wheat but this has been refused, and she has sought other medical advice.

The third case was a primipara, thirty-one years old. There was no family nor personal history of allergic sensitivity. She gave a history of poor heat tolerance

FETAL AND MATERNAL MORTALITY IN DIABETES*

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PRIOR to the discovery of insulin, agreement was uniform that pregnancy constituted a dangerous and undesirable complication of diabetes mellitus. The literature before 1923 is filled with discussion and case reports concerning the harmful effect produced by pregnancy. Few diabetic women bore children (pregnancies in 2 per cent, 5 per cent, 6 per cent of diabetic women of childbearing age as reported by Skipper, Van Noorden, Lecorche), but when a patient did become pregnant her diabetes became more difficult to control, she was very likely to develop acidosis and her chances of surviving the pregnancy were much less than for normal women. The likelihood of obtaining a liveborn infant capable of surviving the neonatal period was less than 50 per cent. The cause of the high fetal death rate was due to many factors. Spontaneous abortions in the early months were attributed to an abnormal endometrium, to variations in maternal blood sugar or to ketosis. Therapeutic abortions were necessitated by increased difficulty in controlling the blood sugar level in the presence of pregnancy. Hydramnios was a frequent occurrence (12 of 66 pregnancies in diabetes collected from the literature by Williams in 1909) and was usually associated with death of the fetus (83 per cent of Williams' 12 cases). The excessive development which frequently occurred if the fetus survived until term was responsible for a greater incidence of intracranial injury than occurs in infants of normal size. A higher incidence of malformations in infants born of diabetic mothers was reported by Joslin, but has not been corroborated by other investigators. Ketosis and abnormal products of metabolism circulating in the mother's blood were regarded as frequent causes of intrauterine death. Hypoglycemia after birth, caused by an overly active fetal pancreas, developed in response to low maternal pancreatic function, was considered a frequent cause of death in the early neonatal period.

One of the first large series of cases of pregnancy in diabetes mellitus collected from the literature was reported by Williams in 1909. In this group of 66 pregnancies, 57 occurred in diabetic women and the first symptoms of diabetes developed after conception occurred in 9. Contrary to more recent observations the mortality was higher in the latter group than in the first. Of the 9 patients with the onset

*This work has been partially conducted under a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

For the first two and one-half years, an ether-extracted oil was used, since that only a cold-pressed oil. Of the 127 patients one has developed malignancy. She revealed chorionepitheliomatous change in what was grossly an hydatid mole found ten months after the termination of a pregnancy in which she had been given an ether-extracted wheat germ oil in small doses for the final six weeks.

Rowntree's report suggests a certain species specificity in the rat for his oil-produced tumor. He and his colleagues did not find such tumors produced with cold-pressed wheat germ oil. Moreover they found the tumors developed in the susceptible species only upon administration of oil containing sediment and when the oil was given in doses enormously greater in proportion to weight than have ever been fed to human beings. As rancidity, which rapidly destroys vitamin E, did not affect the sarco-genic power of their oil, it appears that the vitamin itself cannot be blamed for the production of the neoplasms.

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Trichomonas vaginalis locally infects the vagina. Without appropriate specific therapy, however, a progressive ascending infection of the genital tract ensues with the flagellates following the endometrium and the endosalpinx, or the lymphatics. Such upper genital tract infection rarely causes temperature elevations higher than 39° C.

Pelvic abscesses caused by *trichomonas vaginalis* are not rare. They are characterized by extensive and very dense adhesions. The histologic picture in adnexal disease caused by *trichomonas vaginalis* is not specific and resembles that seen in chronic purulent salpingitis.

The author states that by microscopic examination and by culture it has been possible to determine the presence of *trichomonas* in human sperm, endometrium, chronically inflamed tubes, ovarian cysts, the peritoneum, the blood stream of patients, and the viscera of the fetus.

ARNOLD GOLDBERGER.

there were 5 abortions, including 2 therapeutic, but does not give the number of live births. He has collected 238 cases from other authors in which there were only 114 infants alive three days postpartum (50 per cent). There were 8 maternal deaths during the puerperium, 17 within one year and 19 up to three years, making a total of 14.2 per cent.

Joslin's series of cases (1935) is the largest reported by a single investigator since insulin has been available and consists of 122 pregnancies in which the outcome is known. In only 57 per cent of the cases did the fetus survive. If 13 therapeutic abortions are excluded, the percentage rises to 70 per cent (live births 70, stillbirths 19, miscarriages or abortions 19, therapeutic abortions 13, ectopic pregnancy 1). In 73 patients under Joslin's immediate care the number of live births is 68 per cent, or 75 per cent if 7 therapeutic abortions are excluded. The maternal death rate of 5 per cent is the same as in the pre-insulin era but the cause of death has changed from diabetic coma to obstetric complications. He believes that cesarean section in the early part of the eighth month is the ideal method of delivery.

Since the opening of the present Chicago Lying-in Hospital at the end of May, 1931, until Oct. 1, 1936, 16 pregnancies in 15 women having proved diabetes mellitus have been observed. There have been a total of 14,464 deliveries during this period, making an incidence of approximately one in every 900 deliveries. Eleven women had had symptoms of diabetes for at least two years before the onset of pregnancy, in three it developed during the course of the pregnancy, and in one case the time of onset was unknown. There was only one maternal death (6.6 per cent). This occurred in a woman admitted to the hospital in coma, who had had no prenatal care and who died undelivered a few hours after admission. There were 11 infants (68.7 per cent) alive at the end of the neonatal period. The fetal deaths were due to one therapeutic abortion performed because of the acidosis produced by hyperemesis gravidarum; to one delivery of a macerated stillborn infant in a woman with poorly controlled diabetes; one premature onset of labor at thirty-one weeks due to an unknown cause in which the infant succumbed six hours after delivery, one death of an undelivered infant, and to one death of an infant showing evidence of antenatal pneumonia as a result of premature rupture of the amniotic membranes.

In general, the age when pregnancy occurred is slightly greater than usual, the average age in this group being thirty years. Seven women (50 per cent) showed evidence of toxemia, 5 having relatively mild symptoms and 2 having very severe symptoms. Delivery was natural or aided by low forceps in 7, accomplished by cesarean section in 5; one patient died undelivered and one was subjected to a therapeutic abortion. In the 5 patients delivered by cesarean section the diabetes was considered sufficiently severe to warrant sterilizing the patient at the same time.

The mean weight of the infants delivered at term was 3,935 gm., and the sexes were equally divided. There were no fetal malformations.

The patients were all carefully observed during pregnancy and were, with one exception, very cooperative. The one patient who was delivered

of diabetes during the pregnancy 3 died in coma shortly after labor, 2 died of coma at one and at four months later, 2 died of malignant tumors shortly after labor. Death from diabetes occurred in 55 per cent. Only 3 infants survived, two from mothers who also survived and one from a patient who died of a brain tumor. In the 26 patients (57 deliveries) in whom diabetes was present before conception the mortality during the puerperium was 25 per cent, during the next two years 20 per cent, with a fetal mortality of 49 per cent. Ten of these patients had more than one pregnancy, 6 being apparently entirely unaffected by repeated pregnancies.

Joslin observed 130 pregnancies occurring in diabetic women before the insulin era. Seventy-one per cent of those proceeding to term, in whom the outcome of the pregnancy was known, resulted in liveborn infants. However, from a total of 115 pregnancies (the outcome was unknown in the other 15) there were obtained only 57 live infants (50 per cent). There were 23 stillbirths, 23 abortions and miscarriages, 5 therapeutic abortions, 7 deaths because of deaths of undelivered mothers. The maternal mortality is given as 5 per cent, all deaths being due directly to diabetes.

Since the advent of insulin many more cases have been reported in which diabetes complicates pregnancy.

Fischer believes this indicates that more diabetic women are becoming pregnant. This belief is supported by Skipper's figures which show that of 367 married diabetic women under forty-six years of age only 2 per cent of 190 observed prior to 1922 were pregnant, while 15 per cent of 177 observed since 1922 were pregnant. In spite of the fact that early diabetes is probably recognized more frequently than it was in the past, these figures show that the fertility of a diabetic woman is probably increased by insulin.

Wilder and Parsons (1928), in their study of the effect of pregnancy on diabetes, state that in their experience no patient is permanently harmed by pregnancy if the disease is properly treated. They report 9 cases of pregnancy in diabetes with 6 living children (66½ per cent). The deaths include one infant stillborn at term in a case of neglected diabetes, and 2 abortions at two and seven months from coincidental causes. There was no maternal mortality. An investigation of 51 published case histories from 1923 to 1928 shows 57 per cent living babies with a maternal mortality of 13.7 per cent (7 deaths).

Skipper (1933) reports 37 pregnancies in 33 women with a fetal mortality of 40.5 per cent (including 3 therapeutic abortions), with no maternal mortality during labor or the puerperium and with but one death inside of two years. His figures, collected from the literature on 136 pregnancies in 118 women, show a fetal death rate of 45.2 per cent (abortions, stillbirths, neonatal deaths) and a maternal death rate of 9.3 per cent during pregnancy or the puerperium, with an additional 3.4 per cent dying within two years after delivery.

Ronsheim, between 1920 and 1933, observed 36 pregnancies in diabetic women with only 13 live births (36 per cent), the deaths including 8 therapeutic abortions, 13 stillbirths, and 2 miscarriages. There was only one maternal death. He states that uncontrolled diabetes invariably results in miscarriage, premature birth, or death in utero a few weeks before term. Cesarean section a few weeks before term may occasionally be indicated in the interest of the patient.

Duncan and Fetter (1934) report 6 pregnancies in 5 diabetic women with no fetal or maternal mortality.

Kramer (1935) in 17 patients with 20 pregnancies observed no maternal deaths during pregnancy or the puerperium and only one within two years. He states

TABLE I. PREGNANCY IN PATIENTS WITH DIABETES MELLITUS OBSERVED AT THE CHICAGO LYING-IN HOSPITAL

	DATE OF DELIVERY	AGE AT DELIVERY	DURATION OF DIABETES	SEVERITY OF DISEASE	IN-SULIN	MODIFIED DIET	TYPE OF DELIVERY	COMPLICATIONS	PREVIOUS PREGNANCIES		FETUS	
									BEFORE DI-AGNOSIS	AFTER DI-AGNOSIS	SEX	WEIGHT IN GRAMS
1	1931	27	5 yr.	Sev.	+	+	Ces. sec. steril.	Mod. hypertension	0	0	F	3,010
2	1932	23	2 yr.	Sev.	+	+	Ces. sec. steril.	Yeast infection; pre-eclampsia; hydramnios	1 LB	0	M	4,550
3	1932	30	5 yr.	Mod.	+	+	Spont.	Pre-eclampsia	0	0	F	4,015
4	1933	36	10 yr.	Sev.	+	+	Spont.	Diabetes poorly controlled	1 LB	1 SB 1 LB	F	3,945
5a	1934	36	2 yr.	Mod.	+	+	Spont.	Syphilis (latent); hypertension	4 LB	1 Ab	F	4,000
5b	1935	37	3 yr.	Mod.	+	+	Ces. sec. steril.	Syphilis (latent); hypertension; yeast vaginitis; pre-eclampsia	4 LB	1 Ab 1 LB	M	4,685
6	1934	38	Preg.	Mild	0	+	Spont.	Mild toxemia	1 LB	0	F	3,610
7	1934	22	Unknown	Sev.	+	-	Undel.	Toxemia	5 Ab 1 LB	0	F	?
8	1934	26	6 yr.	Mild	+	+	Low fore.	Mild toxemia	1 LB	1 Ab	M	3,470
9	1935	30	8 yr.	Sev.	+	+	Ces. sec. steril.	None	2 LB	1 LB 2 Ab	M	3,925
10	1935	29	10 yr. No symptoms for 9 yr.	Mild	+	+	Spont. 31 wk.	Premature onset of labor	0	0	M	1,820
11	1936	35	4 yr.	Mod.	+	+	Ces. sec. steril.	Pre-eclampsia	1 LB	0	F	4,320
12	1936	34	4 yr.	Sev.	+	+	Ther. ab. at 2 mo.	Hyperemesis gravidarum	0	0	-	-
13	1936	22	Preg.	Mod.	+	+	Low fore.	None	0	0	M	3,665
14	1936	17	Preg.	Mild	0	0	Low fore.	Well compensated mitral stenosis	0	0	M	3,330
15	1936	36	3 yr.	Mod.	+	+	Embryotomy	Obesity	1 Ab	2 Ab	M	3,510

LB=Normal live born infant.

SB=Still-born infant.

Ab=Abortion.

of a macerated infant found it very difficult to adhere to an accurately planned diet because of financial embarrassment. With the exception of two patients insulin was given during all or the greater part of the pregnancies.

DISCUSSION

Since the advent of insulin the entire management of diabetes has changed. It is no longer invariably fatal even when the onset of the disease is in childhood. The surgical risk to the patient has been markedly lowered, and the average diabetic patient who follows the advice of a competent physician has a life expectancy not greatly below that of the nondiabetic individual. The diabetic patient's reaction to pregnancy must necessarily also be modified by the present accessibility of insulin.

The varying nutritive requirements during pregnancy make it imperative that a diabetic patient be more closely supervised than is otherwise necessary. If her blood sugar level is not constantly controlled by diet and insulin, her outlook is no better than it would have been in the pre-insulin period. Hyperemesis gravidarum may make it impossible to prevent acidosis in a diabetic patient and is a more serious complication than in a nondiabetic. This is one of the few conditions in diabetes in which therapeutic abortion may be necessary.

The published opinion of various writers differs as to the possible effect of pregnancy on the mother, but from a careful study of many of the cases reported, it seems warranted to draw the following conclusions. Pregnancy constitutes an additional strain on an organism already handicapped by an abnormal sugar metabolism. As in any disease, unnecessary additional factors constituting in themselves a risk to the patient are to be avoided if possible. For this reason, if no other conditions are taken into account, pregnancy is to be avoided. If, on the other hand, the patient is anxious to bear children and is able to have her dietary and insulin requirements carefully controlled, there is no evidence to indicate that she will be certainly and permanently harmed by the pregnancy. Death from coma, which was the usual cause in pre-insulin days, is extremely uncommon. (Joslin observed none in 138 pregnancies.) There is a slightly greater risk of toxemia or eclampsia occurring, for the incidence is higher in diabetic than nondiabetic patients, but appropriate treatment may be instituted. Here, as in all patients, careful observation and the discovery of the impending toxemia is the important factor in preventing casualties.

The number of fetal deaths in the series of cases compiled from the literature remains high (see Table II). This is partly due to the inclusion in the statistics of all abortions and miscarriages both uninten-

to the increased amount of available food material occasioned by the maternal hyperglycemia. Fischer (1935), in analyzing birth weights of 49 infants born of diabetic mothers prior to 1922, found 26 (53 per cent) weighing over 4,500 gm. In 31 infants born of diabetic mothers treated with insulin, there were only 5 which weighed 4,500 or more grams (16 per cent). In none of the patients was pregnancy prolonged. (Kaern, in analyzing 26,644 unselected births, found an incidence of only 0.92 per cent with a birth weight over 4,500 gm. and in half of these the period of gestation was over 291 days.) In all infants over 4,500 gm. the death rate is considerably higher than in those whose weight is within normal limits.

Hypertrophy of the islands of Langerhans in the fetal pancreas, caused by insufficiency of maternal insulin, has been reported by several investigators (Gordon, Heiberg, Skipper, Dubreuil and Anderodias, Feldman, Ambard, Wiener). Whether or not insulin passes through the placenta into the maternal blood stream and thereby partially compensates for the lack of insulin in the maternal organism has not been definitely proved. The hypothesis that after birth the excess of insulin, no longer being able to escape through the placental circulation, is sufficient to cause hypoglycemia and death of the fetus is an interesting possibility. It is almost impossible to estimate accurately the island tissue in the fetal pancreas. In one case discovered by us in routine autopsy investigation, the fetal pancreas was composed largely of islands, all of which were several times the normal size. The infant succumbed from pneumonia and the mother showed no evidence of diabetes.

Positive knowledge as to the cause of death in the infants born of diabetic mothers is still lacking. This is partly because any investigator has the opportunity of studying only a limited number of cases, and partly because the cause of death is largely from physiologic disturbances and does not produce demonstrable pathologic lesions.

As the general care of the diabetic patient is improved, the fetal death rate will decrease correspondingly. The diabetic woman's chances of becoming pregnant, of having an uneventful pregnancy and delivering a normal child have been greatly increased by the use of insulin. The more nearly normal her metabolic processes can be made the more normal will be her course and the better the prognosis both for her health and that of the infant.

CASE HISTORIES OF PREGNANT DIABETIC WOMEN TREATED AT THE CHICAGO LYING-IN HOSPITAL

CASE 1.—(47668) Patient, aged twenty-seven, para i, gravida ii. Normal pregnancy in 1925 with first symptoms of diabetes in 1926. Insulin requirement both before and during pregnancy varied greatly from time to time with a maximum dose of 70 units daily. Delivery at term of a 3,010 gm. female infant by cesarean section with accompanying sterilization Nov. 9, 1931. Complication: moderate hypertension. Mother and infant discharged in good condition.

tional and therapeutic. Adair and other investigators have found that among women in general approximately one-third of all pregnancies end in abortions. The incidence is not greater than this in diabetes, so although we may in this group ascribe a reason for the abortion where ordinarily it is very difficult, the incidence in general is no higher than among women in the nondiabetic group.

TABLE II. PUBLISHED MATERNAL AND FETAL MORTALITY RATES IN DIABETES MELLITUS

	YEAR PUB- LISHED	NUMBER PA- TIENTS	NUMBER PREG- NAN- CIES	*FETAL MOR- TALITY %	MATERNAL MORTALITY PER CENT		
					DURING LABOR	FOL- LOW- ING 2 YEARS	TOTAL
Williams	1909	43	66	49.0	25.0	20.0	45.0
Joslin	1935 ¹		115	50.0	5.0		5.0
Parsons and Wilder	1928	9	9	33.0			
Parsons and Wilder†		43	51	47.0			12.0
Skipper	1933	33	37	40.5		3.03	
Skipper†		118	136	45.2	9.3	3.4	12.7
Ronsheim	1933		36	64.0	2.8		2.8
Duncan and Fetter	1934	5	6				
Kramer	1935	17	20			5.0	5.0
Kramert†			238	50.0			14.2
Joslin ²	1935		122	43.0			5.0
Chicago Lying-in Hospi- tal (present series)	1936	15	16	31.3	6.6		

*Includes abortions both spontaneous and therapeutic, stillbirths and deaths during neonatal period.

†Cases collected from the literature by the author.

¹Cases observed prior to the use of insulin (1922).

²Cases observed from 1922 to 1935.

If the deaths of previable fetuses are excluded in the Chicago Lying-in series, there are only 3 deaths in 14 pregnancies, a mortality rate of 21.4 per cent. In 81 patients under Joslin's immediate care, 88 per cent of infants delivered at term were liveborn.

In the infants surviving until term the outcome depends largely on the degree to which the maternal diabetes has been controlled. If the patient's urine has been kept relatively sugar-free by diet and insulin and acidosis has not occurred, a live-born infant, within normal limits of size, will probably be delivered naturally. If the diabetes has not been controlled, the outlook is the same as it was in the pre-insulin era; the infant may succumb before delivery and may show maceration of varying degree, it may attain an abnormal size and die as a result of birth trauma, or it may be apparently normal at the time of delivery and succumb soon afterward. Death shortly before labor is probably due in the majority of cases to transmission from maternal to fetal circulation of abnormal metabolic products which interfere with the normal physiology of the infant. Abnormal size of the infant is believed due

nancy. Medical induction followed by delivery at term (Dec. 3, 1934) by low forceps. Male infant, weight 3,470 gm. Complication: mild toxemia. Mother and infant discharged in good condition.

CASE 9.—(29871) Patient, aged thirty, para iii, gravida vi. Normal delivery in 1924 of 3,600 gm. infant, in 1926 of 3,150 gm. infant, in 1931 of 4,300 gm. infant; 2 unintentional abortions. Onset of diabetes in 1927, with dietary regime followed only moderately well since then; insulin requirement variable with maximum of 50 units. Delivered at thirty-eight weeks' gestation by cesarean section on Mar. 28, 1935. Sterilized. Infant normal, weight 3,925 gm.

CASE 10.—(125560) Patient, aged twenty-nine, para 0, gravida i. Glycosuria accidentally discovered in 1925, disappeared on slight modification of diet and did not reappear until Dec. 19, 1934, when patient was three months pregnant. Diet of protein 60, carbohydrate 150, fat 100 and 15 units of insulin was sufficient to prevent glycosuria. Delivered naturally Apr. 22, 1935, at thirty-one weeks' gestation. Infant died after two hours. Autopsy showed prematurity, slight hyperplasia of islands of Langerhans. Weight 1,820 gm.

CASE 11.—(74337) Patient, aged thirty-five, para i, gravida ii. Delivered one normal infant, date unknown. Onset of diabetes in 1932, controlled by diet and an average of 20 units of insulin. This was increased to 45 units by the thirty-second week of pregnancy, 70 units in the last four weeks, 60 units at term. Delivered by cesarean section Jan. 18, 1936. Sterilized. Normal female infant, weight 4,320 gm.

CASE 12.—(1312) Patient, aged thirty-four, para 0, gravida i. Under observation of medical department since onset of diabetes in 1932. Despite a strict diet the insulin ranged from 20 to 90 units. She became pregnant in November, 1935, and had such marked nausea and vomiting that acidosis developed. Because of the difficulty in controlling the diabetes in the presence of the complications of pregnancy a partial hysterectomy was performed Feb. 13, 1936. Discharged with diabetes well controlled.

CASE 13.—(146114) Patient, aged twenty-two, para 0, gravida i. Onset of symptoms during pregnancy. Placed on strict diet. Insulin required until last month of pregnancy. Delivered with aid of low forceps Apr. 18, 1936, of a normal male infant weighing 3,665 gm. Mother and infant discharged in good condition.

CASE 14.—(145185) Patient, aged seventeen, para 0, gravida i. No symptoms of diabetes; during pregnancy urine showed 1+ to 4+ sugar, during last two weeks sugar in urine glucose tolerance tests both before and after labor indicated true diabetes. Delivered with aid of low forceps August 13. Normal male infant, weight 3,330 gm. Mother and infant discharged in good condition.

CASE 15.—(158861) Patient, aged thirty-six, para iii, gravida iv. Three unintentional abortions at three to four months, 1932, 1933, 1934. First symptoms of diabetes in 1933; followed a diet and took approximately 35 units insulin daily for two years. During the last year has had no insulin, has not followed a diet and when urine has been tested was usually 4+. During last two months of pregnancy, when patient consulted clinic, urine was sugar-free on only mildly restricted diet. Patient admitted in first stage of labor, membranes having ruptured seventy-two hours before onset of labor. Fetal heart tones absent on admission. Delivered Sept. 1, 1936, by podalic version and extraction and embryotomy because of uterine inertia. Autopsy examination of the fetus failed to show any abnormality except an infiltration of polymorphonuclear leucocytes into the lung. Weight 3,510 gm.

CASE 2.—(59732) Patient, aged twenty-three, para i, gravida ii. Pregnancy in 1929 complicated by eclampsia with spontaneous delivery of thirty-seven weeks' fetus which died shortly after delivery. First symptoms of diabetes occurred six months later since which time she has been on a moderately restricted diet and an average of 50 units of insulin daily. Insulin requirement varied practically none during pregnancy. She was given a five-hour test of labor at term but since progress was not satisfactory she was delivered by cesarean section with accompanying sterilization on Aug. 26, 1932. Infant, male, 4,550 gm., normal. Complications: yeast infection, hydramnios, severe preeclamptic toxemia.

CASE 3.—(55029) Patient, aged thirty, para 0, gravida i. Onset of diabetes in 1927, controlled by diet and an average insulin intake of 30 units daily. When six months pregnant, insulin requirement was 90 units daily, at time of delivery 45 units. Delivered naturally June 30, 1932. Normal female infant, 4,015 gm. Mother and infant discharged in good condition.

CASE 4.—(65599) Patient, aged thirty-six, para iii, gravida iv. Pregnancies in 1917 with 3,800 gm. liveborn infant, 1926 with 5,800 gm. stillborn infant, 1930 with 4,500 gm. liveborn infant. Onset of diabetes in 1923. Disease controlled largely by diet with only occasional use of insulin. First seen Aug. 17, 1932, when four months pregnant. Impossible to control diabetes adequately because of lack of co-operation of patient. Delivered naturally of a 3,945 gm. macerated female infant on Feb. 19, 1933.

CASE 5.—(97804) Patient, aged thirty-six, para iv, gravida vi. Four normal liveborn infants; 1913, 2,700 gm.; 1916, 4,500 gm.; 1918, 3,600 gm.; 1922, 3,500 gm.; unintentional abortion at six weeks in 1933. First symptoms of diabetes in July, 1932, controlled by diet until July, 1933 when started taking 30 units of insulin; 65 units in January, 45 units in February, none by the end of March. Delivered naturally Apr. 18, 1934. Normal female infant, weight 4,000 gm. Insulin requirement 15 units daily following delivery until became pregnant again. At eight months required 60 units, at nine months 25 units, at time of delivery none. Delivered on Nov. 8, 1935, by cesarean section. Sterilized. Normal male infant, weight 4,685 gm. Complications of both pregnancies: syphilis, obesity, hypertension; of the second only, preeclampsia, yeast vaginitis.

CASE 6.—(106230) Patient, aged thirty-eight, para i, gravida vii. One normal delivery of 5,000 gm. liveborn infant in 1915 followed by 5 unintentional abortions. First seen June 14, 1934, when sugar was discovered in the urine. Sugar tolerance curve showed presence of diabetes mellitus. Blood sugar was controlled by diet of carbohydrate 110, protein 65, fat 100 without the use of insulin. Delivered naturally at term on Aug. 16, 1934, of a 3,610 gm. normal female infant. Complication: mild toxemia. Mother and infant discharged in good condition.

CASE 7.—(112772) Patient, aged twenty-two, para i, gravida ii. One normal delivery in 1931. First seen on admission to the hospital when six months pregnant Sept. 20, 1934, with history of continuous vomiting and absence of fetal movement for five days. Blood chemistry on admission was nonprotein nitrogen 107, chlorides 438, sugar 322, CO₂ combining power 25 volumes per cent. Diagnosis made of diabetic coma. Died undelivered twenty-four hours after admission. Had had no prenatal care and there had been no previous diagnosis of diabetes. Autopsy confirmed diagnosis.

CASE 8.—(99543) Patient, aged twenty-six, para 0, gravida ii, one unintentional abortion in 1930. Onset of diabetes in 1928; controlled by diet and an average of 10 units of insulin daily. Tolerance remained practically stationary during preg-

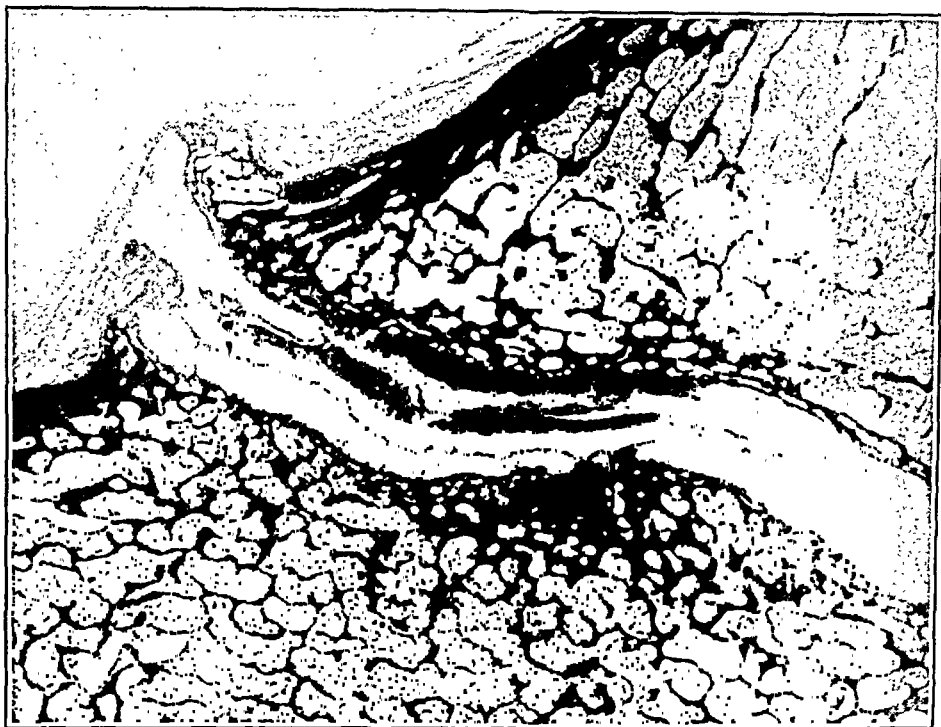


Fig. 1.—Articulatio sacroiliaca of a twenty-seven-year-old woman who had had 2 children. Note the formation of marginal exostoses at the terminal parts of this joint. Hemorrhage has occurred in the joint cavity. (From Lang, F. J. and Haslhofer, L.: Changes in Symphysis Pubis and the Sacro-iliac Articulations as a Result of Pregnancy and Childbirth. Arch. Surg. 25: 870, 1932. Courtesy of Archives of Surgery.)



Fig. 2.—Symphysis pubis of a fifty-two-year-old woman who had had 3 children. The formation of a T-shaped cleft is seen. (From Lang, F. J. and Haslhofer, L.: see above. Courtesy of Archives of Surgery.)

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A ROENTGENOGRAPHIC STUDY OF THE SUPERIOR STRAIT DURING PREGNANCY

PRELIMINARY REPORT

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FOR many years it has been recognized that relaxation of the pelvic joints occurs during pregnancy. The Hippocratic theory of "dis-junctio pelvica" was, perhaps, the vanguard of this recognition. Throughout the ages this phenomenon was intermittently a pivot of controversy and, indeed, Francois Mauriceau in the seventeenth century refused to concede the point.

More recent years have brought out new substantiation of what was once only theory. Roentgenography as applied in obstetrics has played an important part in reactivating an interest in the mobility of the symphysis pubis and the sacroiliac articulations during pregnancy. It has been demonstrated that cyst formation, fissure formation, and hemorrhage into the joint cavities do occur in the articulations of the pelvis during pregnancy or labor. However, in a large series of obstetric patients, managed properly both antenatally and intranatally, one does not frequently observe symptoms and signs postpartum which are attributable to changes in the symphysis pubis or in the sacroiliac joints. The investigations of Lang and Haslhofer prove, however, that "changes in the sacroiliac joints must be considered occasionally as a cause of the backache so frequent in pregnant women and in those who have had many labors."

The predominant opinion holds that there is a widening of the pubic articulation and a concomitant separation of the sacroiliac articulations.

symphysis pubis and the (2) depression below the fifth lumbar vertebra, i.e., the upper angle of the Michaelis rhomboid. Thoms measures from "a point on the anterior surface about 1 cm. below the upper and anterior border of the symphysis." We have found by careful check upon the skeleton that the midpoint upon the

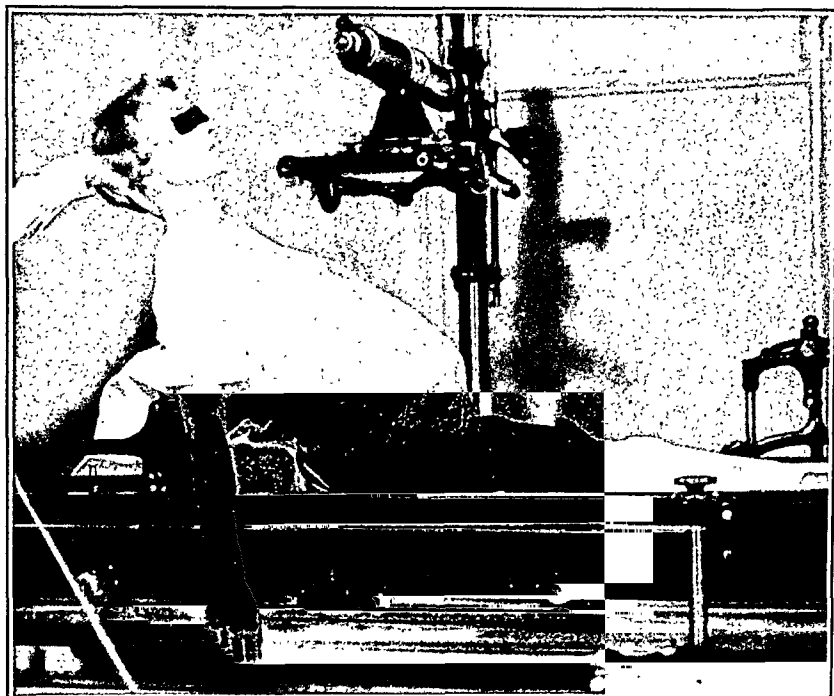


Fig. 3.—Patient in semisitting position, back arched forward by use of sandbag, thus bringing the plane of the inlet into the horizontal.

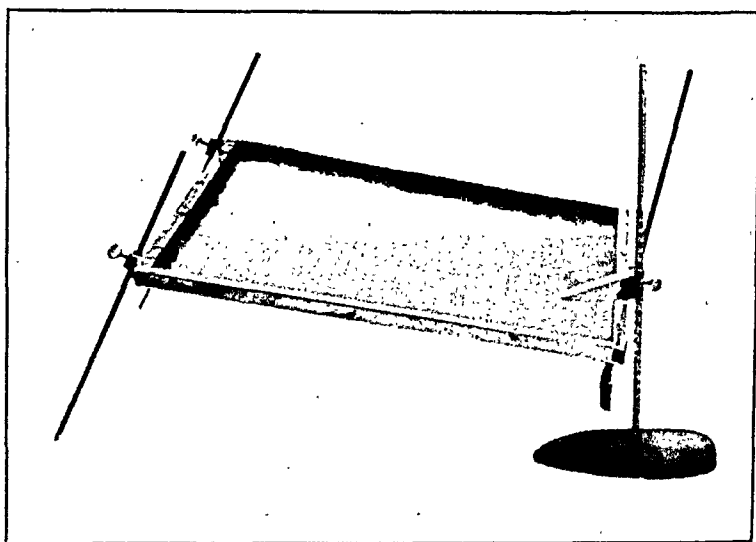


Fig. 4.—Centimeter lead grid on tripod with adjustable legs. Sliding vertical scale for measuring height of symphysis pubis.

superior border of the symphysis is well within constant accuracy for determining the true conjugate by x-ray. This has the advantage of easy identification at any time during pregnancy without danger of error in any given set of determinations.

Before, or at the time of, the first picture the depression below the fifth lumbar spinous process is located and a small wheal of India ink is injected intradermally.

Abramson, Sumner and Wilson state that the average increase in width of the symphysis during pregnancy is 7 or 8 mm. while the maximum is 12 mm. They believe the greatest increase at the symphysis occurs between the fifth and seventh months of pregnancy. Likewise these investigators conclude that no increase in the separation of the symphysis takes place during labor.

Reis, Baer, Arens, and Stewart were unable to demonstrate in 80 consecutive cases, by roentgen examination, any change in the pubic articulation during pregnancy, thus taking issue with Abramson, Sumner, and Wilson. They conclude that any increase in the span of the pelvic articulations takes place only during labor.

Hisaw has demonstrated the presence of a hormone in lower animals which, if injected into virgin guinea pigs, will produce relaxation of the pelvic ligaments. This is, according to Hisaw, a special fraction of the corpus luteum hormone which he named "relaxin." We may therefore conclude, as a basis for this study, that regardless of the time at which separation occurs it nevertheless does take place.

We have inquired as to whether or not this established widening of the joints occurs before labor starts and also whether or not it might favorably influence the outcome of labor especially in contracted pelves. Many an obstetrician has been impressed with the spontaneous delivery of a child through a superior strait which, in early pregnancy, proved by mensuration to be abnormally small. Many have recorded after the first examination and pelvimetry such notes as: "generally contracted pelvis; probable cesarean section," only to be surprised at the ease and rapidity with which the patient delivered.

Since there is relaxation of the symphysis pubis and the sacroiliac joints sometime antenatally, is it sufficient to enlarge the pelvic girdle enough to convert potentially difficult labors into easy ones?

We are able to answer this question at present only with respect to the possible changes which take place prior to the onset of labor. Subsequently we shall attempt to make similar determinations during labor.

This preliminary report is based upon measurement of the inlets of 25 women. No selection as to age, parity, or constitutional type was made. No study was undertaken, however, later than the sixteenth week of pregnancy. Our method is a modification of the Thoms technique of "applying roentgenometric methods of diagnosis to the problems of pelvimetry." While Thoms, Jarcho and others have established the most accurate method of taking simple pelvigrams, this study involves making two radiographic determinations on each patient: one early in pregnancy and another, under identical technical conditions, near term. Such a dual technique obviously opens the way for errors and both exposures on each individual patient must be identical in all conditions as is humanly possible.

METHOD

Our technique consists first of permanent localization of landmarks in each patient. These points are the (1) central point of the superior margin of the

is made as usual through this grid to imprint the dots upon the film making certain that the x-ray tube has not been moved since its adjustment for the radiograph of the patient.

Radiograph time of exposure varied with the patient. In the early pregnancy films two to three seconds was sufficient, but the films taken at term required four to six seconds' exposure due to the great thickness of soft tissue penetrated. All other technical factors remained the same with the entire series of patients.* The same person (D. J. T.) made all of the adjustments of the patients upon the x-ray table and made all of the measurements. This reduced human error to a minimum.

The only pelvic diameters commanding our attention in this study were the true conjugate and the transverse conjugate. We have not considered the bispinous diameter because the plane of the spines lies far enough below the plane of the inlet to admit error due to divergence of the x-rays. An approximation of this diameter, however, is of practical value where it is of serious consideration.

Figs. 5 and 6 show a typical pair of pelvigrams. The first film was taken at fifteen weeks of pregnancy. The second film was secured at the thirty-ninth week of gestation. In the earlier determination the conjugate vera and the transverse conjugate are 11.5 cm. and 12.5 cm., respectively, while in the second radiogram these dimensions are, respectively, 11.25 cm. and 12.5 cm. Thus, no enlargement in the area of the superior strait is demonstrated.

Table I presents actual measurements of the conjugate vera and of the transverse diameter in 10 of the 25 women. "A" represents the

TABLE I

PATIENT	WEEKS OF GESTATION	DIMENSIONS	
		CONJ. VERA	TRANS. DIAM.
1	A 12	12.0 cm.	12.0 cm.
	B 36	12.5	13.0
2	8	12.0	11.8
	38	12.5	12.0
3	15.5	11.0	11.25
	38.5	11.25	10.75
4	14.0	12.0	14.5
	39.5	11.75	14.0
5	13	11.5	12.25
	39	12.0	12.5
6	14	13.0	14.5
	41	13.0	14.0
7	9	11.25	11.5
	41	12.0	11.75
8	16	12.5	13.0
	37	12.5	13.0
9	15.5	13.0	13.5
	38	13.75	13.5
10	10	13.25	13.0
	39.5	13.0	13.0
AVERAGES TAKEN FROM 25 CASES		11.9	12.7
		12.0	12.8

*All radiograms were made with General Electric x-ray equipment (KX No. 1); Potter-Bucky diaphragm at 30 inches distance; General Electric XP tube with 100 M. A. using 76 Kvp.

With care, this may be done without disfigurement and has the advantage that months later the same landmark exists from which to measure when the second film is taken.

The patient is placed upon the table in a semirecumbent position with the lumbar spine arched forward in order to reduce the angulation which the plane of the

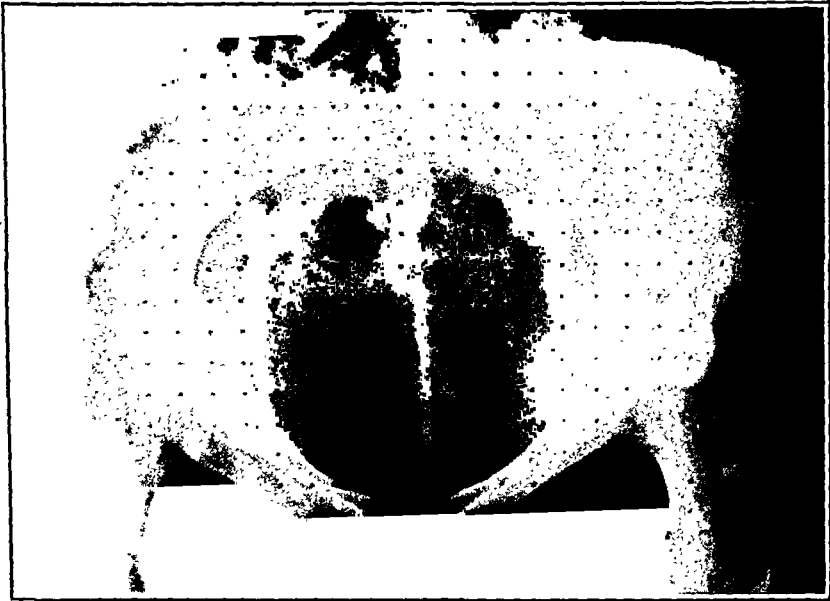


Fig. 5.—Sixteen weeks pregnant. Conjugate vera: 11.5 cm. Transverse conjugate: 12.5 cm.

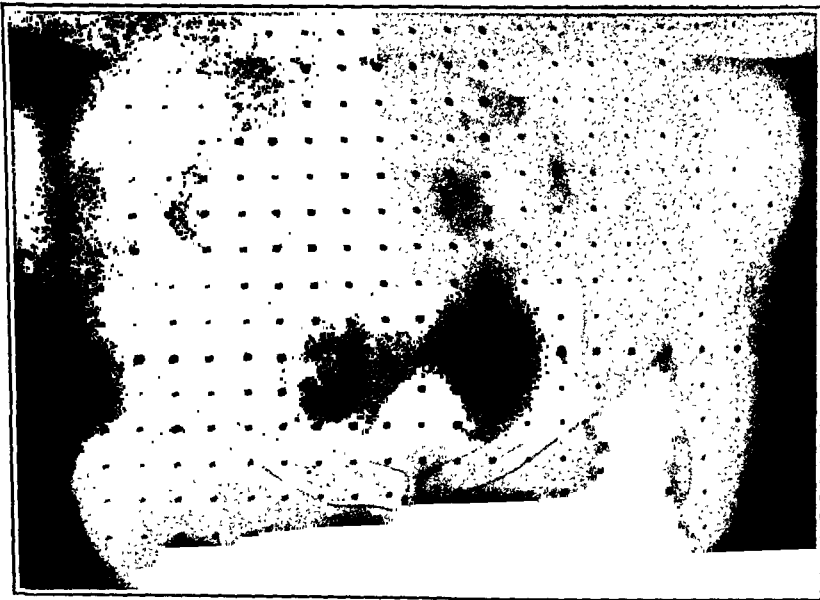


Fig. 6.—Same patient as in Fig. 5; thirty-nine weeks pregnant. Conjugate vera 11.25 cm. Transverse conjugate: 12.5 cm.

inlet makes with the plane of the table surface (Fig. 3). The method of determining distances from the symphysis and the posterior landmark is essentially that of Thoms and Jarcho. When the patient has been x-rayed and has been removed from the table, the centimeter lead grid is placed accurately in the same position occupied by the plane of the superior strait (Fig. 4). A flash exposure

3. Radiographic studies of exactitude reveal no definite and reliable increase in the capacity of the pelvic inlet or superior strait.

4. Erroneous conclusions may be drawn concerning cephalopelvic proportion or disproportion from radiograms of the superior strait taken with the subject in the supine or prone positions.

5. The possibility of an increase in the dimensions and capacity of the superior strait during actual labor is to be studied subsequent to this report.

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MEDICAL-DENTAL BUILDING

DIABETIC OR MYCOTIC VULVOVAGINITIS

SUPPLEMENTARY REPORT

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IN 1933 a preliminary report¹ from a study of 21 diabetic (diabetes mellitus) patients with "diabetic vulvitis" indicated that fungi were the etiologic agents. At that time only impressions were given as the number of patients was too small to draw conclusions, but since then an additional 37 patients with "diabetic vulvitis" have been studied. This gives in all 58 diabetic patients with vulvitis and pruritus. Simultaneously 53 diabetic females without vulvitis and/or pruritus and 38 "control" individuals were observed, cultured, and tested. Thus the grand total is 149, of which 111 were diabetic patients; of the 111 patients 97 were adults and 14 preadolescents. The results not only confirm the original impressions but show most convincingly that the etiologic agent of "diabetic vulvitis" is usually, if not always, a fungus. Furthermore, a slight correction will be made regarding the particular type of fungi responsible for this inflammatory process.

Until 1931, when Plass, Hesselstine, and Borts² pointed out that diabetes is a predisposing factor for such infections, the modern American gynecologic textbooks and other publications had not indicated that fungi were etiologic agents of "diabetic vulvitis." Foreign literature was of the same tenor. On the other hand, vulvovaginal mycoses were recognized by Mayer,³ von Winckel,⁴ Haussmann,⁵ and

first radiogram taken and the gestation in weeks. "B" represents the second radiogram and the number of weeks of gestation.

One-half centimeter, plus or minus, may be accurately allowed for error in technic. This is according to Thoms' experience, and we also have found the same latitude permissible in radiographic experiments upon the skeleton. This explains the apparent "shrinking" of an occasional dimension in the later films. Furthermore, none of the numerical increases in the dimensions of the inlet at term can be considered actual increases. Certainly one cannot conclude that there is an increase of the dimensions of the superior strait during pregnancy which will facilitate an otherwise slow and difficult labor. There is no expansion of the area of the inlet prior to the onset of labor.

Attention is directed in Fig. 7 to the fallacy of taking x-rays with the patient in the supine or prone positions to secure information

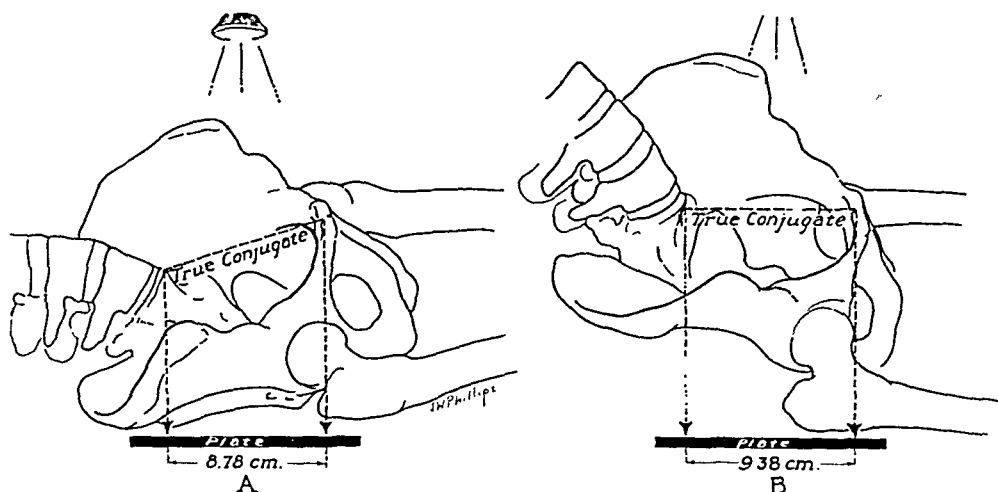


Fig. 7.—True conjugate on skeleton drawn to scale. A shows erroneous figures (8.78 cm.) with patient in prone position. B shows actual figures (9.38 cm.) when inlet is parallel to table.

upon the size of the inlet. These two figures were drawn exactly to scale. The values inscribed are the actual measurements of the true conjugate on a skeleton. Note the orthographic projection of this dimension in Fig. 7-A when the subject is supine, and the shortening of the projected delineation upon the radiographic film. Fig. 7-B represents a true dimensional projection of the conjugate vera upon the film and reveals an increase of 0.6 cm. over the fallacious value in Fig. 7-A.

CONCLUSIONS

1. There has been for many years a supposition that throughout pregnancy an enlargement of the pelvic inlet occurs.

2. Relaxation of the so-called pelvic joints during pregnancy is definitely established but such relaxation is of no apparent value in cases of dystocia involving the superior strait.

base. One may gather the impression that the vulva appears "cooked" or "boiled." The appearance of the vulval mycosis may resemble closely an early chronic atrophic dermatitis of the vulva (kraurosis) as has been illustrated by Adair and Davis.²² In atypical cases the surface may appear to be acutely inflamed, while in some mild cases very little reaction takes place. In the chronic cases hypertrophy of the epithelium and even pigmentation may occur. The not uncommon secondary bacterial invasion may produce a chronic dermatitis. Thus the appearance of "diabetic vulvitis" and mycotic vulvitis are identical.

The symptoms of "diabetic vulvitis"⁶⁻¹² and mycotic vulvitis^{1, 2, 17, 20} are also alike. The only constant symptom is pruritus. Other symptoms of tenderness, pain, discharge, heat, etc., are variable and not necessarily related to the severity of the reaction. Some patients report that the pruritus may be so compelling that scratching is avoided only with difficulty. Patients may awaken themselves from deep sleep to find that the vulval epithelium has been broken and injured by extensive scratching. No vulval itching can be more severe, chronic atrophic dermatitis not excepted. Fortunately most patients with mycotic vulvitis do not have such severe symptoms.

Originally the diagnosis of "diabetic vulvitis" was made by observing this characteristic vulvitis in a diabetic patient. Usually these patients had a moderately severe glycosuria, but even in the absence of "glucose spill" it has been assumed that there might be some causative irritating substances (other than glucose). The clinical diagnosis of a vulval mycosis is made by the characteristic appearance alike in diabetic and nondiabetic patients. There may be a vaginal mycosis with thrush patches or caseous material along with the vulvitis. The diagnosis of either is easily verified by finding fungi in direct smears or on cultures of Sabouraud's media (Plass and others).² Incubation at 37° C. for twenty-four to forty-eight hours is usually sufficient time. The fungi grow by the formation of spherical or oval buds or conidia and in some instances by mycelia. These units are very distinctly gram-positive. The buds are about as large as white cells but are easily distinguished. The mycelia are long, heavy structures. The junctions present somewhat the appearance of the joints of a bamboo stalk. The mycelia may branch and conidia grow at the junction or terminal portion.

In the study of these 111 diabetic patients (Chart 1) and 38 control individuals, cultures were made routinely on Sabouraud's medium. Ordinarily, only single but well-planted cultures were obtained from each patient. One might suggest that such routine would fail to give a large incidence, especially in the control series, but it has been learned from experience that the error is only slight in the hands of one accustomed to this type of investigation.

It has been demonstrated by Plass and others² that yeastlike fungi may be recovered from the vulva and vagina of apparently normal adults, yet Hesselatine and others²³ have shown that these same organisms, although pathogenic for some, are not disease-producing in all instances.

others in the latter part of the nineteenth century, and many of the modern textbooks of gynecology⁶⁻¹⁴ give brief reference to the infrequency and mildness but do not correlate predisposing and precipitating factors. Le Blaye,¹⁵ Davis,¹⁶ Popoff, Ford, and Cadmus,¹⁷ Odland and Hoffstadt,¹⁸ and others report in the recent literature that the disease is not common and is generally mild. The reports of Wong and Kurotchkin,¹⁹ Karnaky,²⁰ Hesselstine,¹ Woodruff and Hesselstine,²¹ Plass and coworkers,² and others indicate a frequent incidence. They point out the possibility of severe irritation in a few patients while some have little distress and others may even be symptomless carriers.

The relation of vulvovaginal mycoses caused by the yeastlike fungus to available glucose has not been sufficiently stressed. In diabetes the frequent spill of glucose over the vulva would produce a more favorable environment even if there was not an appreciable alteration in the cellular carbohydrate content. In pregnancy a similar environment might result from the unusual accumulation (normally) of the glycogen-like substances in the vaginal epithelium, which in turn is converted into utilizable (carbohydrate) materials as the epithelium is cast off and broken down.

The name "diabetic vulvitis" was given because of the rather characteristic clinical entity observed not infrequently in diabetic females, because the onset or exacerbation was so often related to an increase in glycosuria, and because clinical improvement often occurred after control of the diabetes. Such reasoning did not explain the occasional persistent vulvitis following proper diabetic management or the clinical improvement produced by certain antiseptics (fungicides) before the institution of diabetic management. For many years it was taught that the reaction was brought about by the glucose or irritating substances in the urine, and many texts still so state.

If "diabetic vulvitis" is a mycosis one should (a) be able to secure positive fungous cultures, (b) fail to reproduce the symptoms or tissue change by applying the various substances in the diabetic urine to the vulva in the absence of fungi, and (c) show that vulval mycosis presents the same clinical features. The tables and explanations fulfill conditions of (a) and (c) and part of those of (b).

Plass and coworkers,² and Hesselstine¹ have described the following vaginal and vulval changes due to yeastlike fungi. The vulva is slightly swollen, tender, with a reddish blue under-color and a thin, grayish surface. The epithelium appears definitely injured. Abrasion or excoriation may have resulted from scratching. There is an increase of local heat subjectively, and the area is warm to touch. The area most often involved extends from the hymenal ring, or slightly above in some instances, outward. It usually remains limited to the moist surfaces but in the severe cases it extends upward to the mons veneris, outward to the crural fold, and posteriorly to encircle the anus. The labia minora with the prepuce show the greatest reaction usually. Some small whitish areas (thrush spots) or caseous material may be observed. If the surface epithelium is rubbed or scraped the superficial portion of the epithelium may be lost over small areas leaving a reddened but nonbleeding

Monilia albicans and *Monilia candida* (Types 2 and 3 of Stovall and Bubolz) with a few atypical strains are the usual fungi present in the vagina.

Because many diabetic females are free from vulvitis it required a few years of cooperation with internists and pediatricians to secure a group of 58 with vulvitis. It will be noted in Table II that prior to 1931 the material was from the University of Iowa while after July 1, 1931 the patients were from either Rush Medical College or the University of Chicago Clinics. Of the 111 the University of Iowa supplied 42, but of this number only 7 had vulvitis and 14 were preadolescent patients. One of the preadolescents had vulvitis, which leaves 22 adults for the control series. At Chicago no premenstrual patients were studied. At Rush 19 cases with and 9 without vulvitis were collected, while from the University of Chicago Clinics 32 with and 9 without vulvitis were cultured. The sexually immature, mature, and postmenstrual groups show little variation.

TABLE I. MORPHOLOGIC COMPARISON OF YEASTLIKE FUNGI ISOLATED FROM DIABETIC PATIENTS WITH VULVITIS TO SACCHAROMYCES (YEASTS) AND ENDOMYCES

	CRYPTOCOCCI	MONILIA	SACCHAROMYCES	ENDOMYCES
Conidia	Round or oval	Round or oval	Round or oval	Round or oval
Mycelia	None	Branched and jointed	None or rudimentary	Branching and jointed
Endospores	None	None	True—2 to 4 usual	True—2 to 4 usual

The 58 patients with vulvitis (Table III) ranged in age from twelve to seventy-three years. The patient of undetermined age was one in mid-adult life. It will be obvious at a glance that a large number of the patients (exactly 36) were in the postmenopausal period, while only 1 was premenstrual and 21 were menstrual. A relationship of parity or nulliparity to the vulvitis is not obvious. All were nonpregnant patients but one, aged thirty-seven years, whose first gestation was of twenty weeks' duration. The term "menstrual" means in the period from menarche to the menopause, while "premenstrual" and "postmenstrual" designate before and after menstrual respectively. There were three of the entire group who had negative fungous cultures. These were aged fifty, fifty-four, and undetermined. The first two had applied antiseptics to the vulva only a few hours before coming to the clinic. The interference in the third patient was menstrual flow contaminating the entire vulva. Unfortunately these patients did not present themselves at the clinic again when the observer and culture material were available.

The age incidence is comparable in diabetic and control groups. The data on childbearing have been confused, but deviation in either direction appears to be of little significance.

The 111 patients are made up of two groups: 58 with vulvitis and 53 without vulvitis. In the group of 58, 55 had positive fungous cultures. The 3 negative ones will be explained in the discussion of Table II. There was only one preadolescent patient in this group. The group of 53 had 13 preadolescent patients. Four adults and one child had positive cultures. These five patients were all without symptoms and had previously been free from vulvitis or irritation.

Table I was devised to show the general morphologic method of identifying the yeast and yeastlike fungi isolated from the human vagina and vulva. In the previous report it was stated that endomyces were

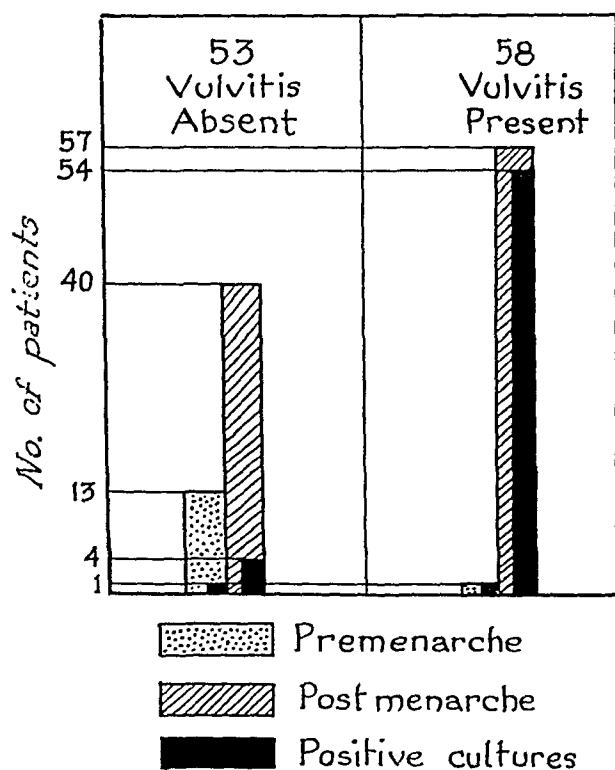


Chart 1.—Incidence of fungi in diabetic females.

recognized. These actually were monilia since vacuoles, or bodies, had been mistaken for endospores in the early study. Repeated fermentation tests and morphologic examinations now definitely confirm the correctness of this last statement for all the strains available from the University of Chicago series. Hopkins and Hesseltine,^{24, 25} using their methods, found only monilia and cryptococci. The monilia definitely predominated. *Saccharomyces* was not found although it has been isolated from the human vagina by other workers. *Endomyces* is an unproved pathogen for the genital tract and so far has not even been isolated from this site. Hopkins and Hesseltine,^{24, 25} in special studies of 81 strains of cryptococci and monilia isolated from oral thrush and vulvovaginal mycoses, proved that Types 1 and 2 of cryptococci and

TABLE III.* DIABETIC PATIENTS WITH VULVITIS

AGE	NUMBER	MATURITY	PAROUS	FUNGUS CULTURE	REMARKS
12	1	Men.	No	+	
13	1	Pre.	No	+	
14	1	Men.	No	+	
16	2	Men.	No	+	
24	1	Men.	Yes	+	
28	1	Men.	No	+	
31	1	Men.	Yes	+	
33	1	Men.	Yes	+	
34	1	Men.	Yes	+	
35	1	Men.	Yes	+	
37	1	Men.	No	+	First pregnancy—5 months
38	1	Men.	Yes	+	
39	2	Men.	Yes	+	
41	2	Men.	Yes	+	
45	4	1 Und. 3 Post.	Yes	+	
47	1	Post.	Yes	+	
48	5	3 Men. 2 Post.	Yes	+	
49	1	Post.	Yes	+	
50	2	Post.	1 Und.	+	
			1 Yes.	-	Antiseptic on vulva
51	1	Post.	Yes	+	
53	2	Post.	1 Und.	+	
			1 Yes.	+	
54	1	Post.	Yes	-	Antiseptic on vulva
56	3	Post.	1 Und.	+	
			2 Yes.	+	
57	3	Post.	1 No	+	
			2 Yes.	+	
59	2	Post.	Yes	+	
60	1	Post.	Und.	+	
61	2	Post.	Yes	+	
63	1	Post.	Und.	+	
64	2	Post.	Yes	+	
65	3	Post.	Yes	+	
66	2	Post.	Yes	+	
69	2	Post.	1 Und.	+	
			1 Yes.	+	
72	1	Post.	Und.	+	
73	1	Post.	Yes.	+	
Undet.	1	Und.	Und.	-	Menstruating

*Pre., Premenacme or prior to menstruation; Men., menacme or menarche to menopause; Post., postmenacme or after menopause; Und., undetermined.

A larger number of diabetic females could have been procured through the courtesy of the medical staffs, but 53 (Table IV) seemed adequate for general purposes when such great differences in the incidence of fungi existed. The total of 53 is made up by 13 premenacmic, 20 menacmic, and 20 postmenacmic patients, all entirely free from vulvitis clinically and symptomatically. It is also interesting to note that one of the 13 immature females, 3 of the women of reproductive age and one of the postmenstrual group had positive cultures for yeast. Those in this control series with positive cultures must be classified as carriers according to the reports of Plass and others,² Woodruff and Hesseltine,²¹ and others. Nineteen of those with negative cultures did admit, when in-

TABLE II.* INSTITUTIONAL SOURCES, SERVICE ASSIGNMENT, AND MENARCHE AGE OF DIABETIC PATIENTS WITH AND WITHOUT VAGINITIS

COURTESY OF		VULVITIS				NO VULVITIS				TOTALS
		PRE.	MEN.	POST.	UND.	PRE.	MEN.	POST.		
University of Iowa† College of Medicine Medical Department 1930-31 Pediatric Department† 1930-31	Drs. F. M. Smith and C. W. Baldrige	0	3	3	0	0	12	10	28	
		1	0	0	0	13	0	0	14	
		7				35				42
University of Chicago Div. Biol. Science Medical Department 1931-36 Rush Medical College Medical Department 1931-33	Drs. Louis Leiter H. L. Schmitz Allan Kenyon Henry T. Ricketts Drs. R. T. Woodyatt L. K. Campbell	0	12	19	1	0	5	4	41	
		0	4	14	1	0	4	5	28	
		51				18				69
Totals		1	19	36	2	13	21	19	111	
		58				53				

*Pre., Premenarche or before menarche; Men., menarche or menarche to menopause; Post., postmenarche or after menopause; Und., undetermined.

†Taken from data of Plass, Hesselstine and Borts.

the 14 had menstruated although several, including those with positive cultures, showed definite evidence of entering or approaching the adolescent stage. Thus, there was one mycotic vulvitis, one fungous carrier,

TABLE V. PREMENACMIC PATIENTS

AGE	NUMBER	FUNGOUS CULTURES	VULVITIS
Undetermined	1	Negative	No
6	2	Negative	No
7	2	Negative	No
9	1	Negative	No
10	1	Negative	No
11	1	Negative	No
12	3	2 Negative 1 Positive	No
13	1	Positive	Yes
14	1	Negative	No
15	1	Negative	No
Totals	14	2 Positive 12 Negative	{1 Vulvitis 1 Carrier—no vulvitis 12 No vulvitis

All from Dept. of Pediatrics—Children's Hospital, Iowa City, University of Iowa,
Courtesy of Dr. P. C. Jeans

TABLE VI. REACTION OF 13 PATIENTS TO GLUCOSE (10 PER CENT) VULVAL DOUCHES (SUBSTITUTE GLYCOSURIA)

AGE	MONTHS PREGNANT	COMPLICATIONS	DAYS OF WASH	TISSUE CHANGE OR SYMPTOMS
<i>Fungi Absent</i>				
20	0	Salpingitis	14	None
22	6	Pulmonary tuberculosis	11	None
22	5	Threatened premature labor	5	None
24	8	Coarctation aorta	3	None
28	8	Hypertension	10	None
28	6	Hypertension	10	None
30	6	Pulmonary tuberculosis	22	None
38	7	Nephritis	11	None
40	8	Habitual abortions	10	None
<i>Fungi Present</i>				
20	8	Cardiac, fungous carrier	5	Sl. injection
24	5	Pulmonary tuberculosis, vaginal mycosis	1	Acute exacerbation
29	7	Threatened premature labor, fungous carrier	1	Severe
37	8	Diabetic, vaginal mycosis	4	Marked

REACTION OF 25 PATIENTS TO GLUCOSE (95 PER CENT) OR LACTOSE (95 PER CENT) WITH CITRIC ACID (5 PER CENT) VAGINAL INSUFFLATIONS*

	FUNGI ABSENT			FUNGI PRESENT		
	NO.	PATIENTS	TISSUE CHANGES OR SYMPTOMS	NO.	PATIENTS	TISSUE CHANGES OR SYMPTOMS
Glucose and citric acid	4	Nonpreg- nant	None	5	Pregnant	Mycosis produced or made worse
Lactose and citric acid	4	Nonpreg- nant	None	12	Pregnant	None
	—			—		
	8			17		

*After Adair and Hesselbine: AM. J. OBST. & GYNEC. 32: 1, 1936.

TABLE IV.* DIABETIC PATIENTS WITHOUT VULVITIS

AGE	NUMBER	MATURITY	PAROUS	FUNGOUS CULTURES	REMARKS
Und. child	1	Pre.	No	-	
6	2	Pre.	No	-	
7	2	Pre.	No	-	
9	1	Pre.	No	-	
10	1	Pre.	No	-	
11	1	Pre.	No	-	
12	4	3 Pre.	No	1+	Carrier
				2-	
		1 Men.	No	-	
14	4	1 Pre.	No	-	
		3 Men.	No	-	
15	1	Pre.	No	-	
	1	Men.	No	-	
16	1	Men.	No	+	Carrier
17	2	Men.	No	-	
20	1	Men.	No	+	Carrier
21	1	Men.	No	-	
26	1	Men.	No	-	Five months pregnant
29	1	Men.	No	+	Carrier
39	1	Men.	Und.	-	
41	1	Men.	Yes	-	
42	1	Men.	Yes	-	
43	1	Men.	Yes	-	
44	1	Men.	Und.	-	
45	2	Men.	Yes	-	
48	1	Post.	No	-	
49	2	Post.	Yes	-	
50	2	1 Men.	Yes	-	
		1 Post.	Yes	-	
52	1	Post.	Yes	-	
53	1	Post.	Yes	-	
56	1	Post.	Yes	-	
58	2	Post.	Yes	-	
60	3	Post.	Yes	-	
61	1	Post.	Yes	-	
64	1	Post.	Yes	-	
65	4	Post.	Yes	-	
70	1	Post.	Yes	+	Carrier
72	1	Post.	Yes	-	

*Pre., Premenacme or prior to menstruation; Men., menacme or menarche to menopause; Post., postmenacme or after menopause; Und., undetermined.

terrogated directly, that they had had vulva irritation at some time previously. Since there are various causes for such complaints and since this complaint was not directly related in all instances to glycosuria, further comments are unnecessary. The age incidence appears unimportant and speaks for itself.

Because particular attention may be focused upon the children (premenacme) Table V was prepared from the previous data. Out of 14 consecutive diabetic patients admitted to the pediatric service (Courtesy of Dr. P. C. Jeans, head of the Children's Hospital in Iowa City) only one admitted vulval irritation, and this was one of two with positive yeast cultures. The vulval appearance conformed to that of a mild mycosis and no other etiologic agent could be found. The other case with positive yeast culture must be classified as a carrier. Not one of

At the Chicago Lying-In Hospital and the University of Chicago Clinics (Max Epstein) diabetes mellitus has been diagnosed in 4 of 32 patients with vulvitis. Consequently, one should suspect all nonpregnant patients with mycotic vulvitis as being diabetics until definite evidence to the contrary is available.

CONCLUSIONS

1. In the presence of monilia or cryptococci the application of glucose in powder or aqueous solution will be associated usually, if not always, with the development of a vulvovaginal mycosis or will cause exacerbations of mycosis.

2. In the absence of yeastlike fungi the application of glucose in powder or aqueous solution has produced no symptoms or tissue changes.

3. The incidence of fungi in diabetes mellitus patients with vulvitis, and the similarity of the clinical appearance of mycotic vulvitis and of "diabetic vulvitis" justifies the previous statement that "diabetic vulvovaginitis is an infection, usually a mycosis, and rarely, if ever, an irritation from products in the urine."

4. Glucose available in the urine or the tissues favors the development of a vulval mycosis, just as its topical application may do.

5. Fungicidal therapy will cure "diabetic vulvitis."

6. Vulval mycosis occurred in diabetic patients from twelve to seventy-three years of age.

7. Whenever mycotic vulvitis is found in a nonpregnant patient one should exclude the possibility of diabetes mellitus.

8. Either "mycotic vulvitis" or "fungous vulvitis" is correct and accurate and should replace the incorrect, misleading and obsolete term "diabetic vulvitis."

9. Even such terms as "aphthous vulvitis," "thrush vulvitis," or "yeast vulvitis," do not conform to the modern taxonomy.

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and 12 without evidence of a vulvitis past or present, as elicited from the patient, the patient's parents, or the referring physician.

The data in Table VI support the previous experimental findings that glucose as such in either aqueous solution or powder is nonirritating. The first portion of the table gives data for those patients without fungi who had 250 c.c. of a 10 per cent aqueous solution of glucose poured over the vulva 5 times daily. The shortest period of exposure was three days in one, and ten or more days in 7. The longest continuous treatment extended to twenty-two days. Perhaps these periods are too short, but when the same glucose solution was poured over the vulva of patients with fungi present, symptoms and findings typical of a mycosis appeared in one to five days. Thus, one must admit that the fungi have some direct relation to the vulvitis. The gestational state and diagnosis are indicated for each patient. According to Hawk and Bergeim²⁶ the urine of diabetic mellitus patients seldom, if ever, reaches 10 per cent glucose concentration or contains over 125 gm. of glucose in twenty-four hours. Thus with 1,250 c.c. used during each twenty-four hours the total of 125 gm. of glucose was washed over the vulva in the control cases without producing or inducing any reaction. Yet when fungi were present the reaction occurred promptly.

The last portion of Table VI was taken from the report of Adair and Heselstine²⁷ on the treatment of vaginal trichomoniasis. The mixture of glucose and citric acid or lactose and citric acid was 95 per cent to 5 per cent, respectively. More recently these sugars, especially lactose, have been used without citric acid and the same responses continue. Karnaky²⁸ reports that glucose induces a mycosis when monilia are present unless some fungicide is added to prevent it. In those cases with fungi present the citric acid did not prevent the exacerbation of the disease by glucose although lactose appeared innocuous.

DISCUSSION

In addition to the data given in two or three instances all vulval irritation was relieved at least partly by using fungicidal therapy before the patient was placed under diabetic management. There have been a few diabetic patients whose vulvitis did not improve with proper diabetic management and the disappearances of the glycosuria, but cures were prompt with fungicidal therapy.

Infrequently one may observe, as was done in this series, instances of the spouse being either the recipient or the disseminator of the fungi. Males appear to be less susceptible than females. The reports of the urologists show that all instances of balanitis occurred in uncircumcised patients.

The source of these yeastlike fungi is probably multiple, but is most likely the hands, clothes, sexual partners, and feces.

chlorides by the method of Volhard and Harvey, and basal metabolism by the Dubois method in duplicate. The raw data are given in Table I.

Serum calcium-calcium balance relations could be studied in various ways. We have used here Pearson's standard correlation technique. Each constituent included in the balance—food, feces, and urine—was related in turn to the serum calcium, the weight gain of the mother, and her oxygen consumption.

The usual method of expressing balance is in net. This method obscures some aspects of the distribution of calcium which seemed pertinent to the question we were studying. Hence, we used a series of ratios in addition to net to see if the movement of calcium through the blood stream and channels of excretion could be studied more clearly from them than from the net. Fraction I, therefore, is serum calcium minus urinary calcium each expressed in milligrams per cubic centimeter. Fraction II is food calcium ingested during the twenty-four hours minus the corresponding fecal calcium, and Fraction III is twenty-four-hour calcium ingestion minus the twenty-four-hour excretion of calcium in the urine.

Basal metabolic rate figures as such of course depend upon the weight, height, and age of the subject. Hence we used the average oxygen consumption per minute during the standard basal test period in these comparisons. This is discussed as *oxygen consumption*. The effects of weight changes upon the net and serum calcium and the oxygen consumption were studied either in relation to weight on the test day or weight gain up to that stage in pregnancy. Urinary phosphorus and chlorine and certain elements of the calcium balance, the serum calcium and basal metabolism were interrelated also.

In making interpretations we arbitrarily grouped the correlations into three categories regardless of the sign of the *r*. Correlations ranging between 0 and plus or minus 0.3 were said to show that the specific items compared were *independent*; if the *r* was plus or minus 0.3 to 0.6 inclusive the items were said to be *somewhat* related, and a correlation of plus or minus 0.6 and above is considered here to indicate a *fair degree* of relationship.

Serum Calcium.—Serum calcium was independent of and therefore not definitely affected by the calcium ingested during these tests. The types and levels of ingestion chosen by the women had varied within the range generally accepted as fairly adequate in quantity. The oxygen consumption and weight or gain in weight had as little relation to it; the same status existed between serum calcium and Fraction III, and either the urinary calcium or phosphorus.

	<i>r</i>	P.E. _r
Serum calcium and calcium ingestion	= -0.16 ± 0.09	
Serum calcium and weight	= -0.03 ± 0.12	
Serum calcium and weight gain	= -0.18 ± 0.08	
Serum calcium and Fraction III	= -0.15 ± 0.09	
Serum calcium and urinary calcium Mg./c.c.	= -0.24 ± 0.11	
Serum calcium and urinary phosphorus Mg./c.c.	= -0.08 ± 0.11	

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ON CERTAIN RELATIONSHIPS OF CALCIUM IN THE BLOOD SERUM TO CALCIUM BALANCE AND BASAL METABOLISM DURING PREGNANCY*

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THE effects of normal pregnancy upon the level of serum calcium and the relation between various forms of calcium ingestion and calcium in the serum have been studied extensively both on the human and on laboratory animals. Few studies are available where the degree of relationship between all the elements of the alimentary balance, serum calcium and basal metabolism have been studied simultaneously during pregnancy and these data therefore are presented to add to information already available about such relationships.

A three-day test period for sampling mineral balances during pregnancy has been studied at Fels Research Institute for the past four years. The findings have been compared with mineral metabolism data collected by using other types of test periods,¹ and the results to date seem to show that some interpretation can be made of trends of mineral and nitrogen metabolism when this method of sampling is used within the limits between which the ingestion of our subjects varied. The subjects of the experiment were shown how to weigh their food and were instructed to eat the same kind and quantity for each of three successive days. On the third day the food was sampled and collections of the twenty-four hour excretion of urine and the feces from the corresponding twenty-four-hour ingestion were made. On the morning of the fourth day blood was drawn for serum calcium immediately after the basal metabolic rate was determined.

Serum calcium was determined by the method of Folin and Wu, balance calcium by permanganate titration after dry ashing all samples, phosphorus on the ashed sample by the method of Embden and Fetter,

*The work was done at the Samuel S. Fels Research Institute as part of a series of studies on metabolism during pregnancy. The writers wish to express their appreciation to Elton Huff and Virginia Torbet for some of the analyses included in the study and to Dr. L. W. Sontag, Director, for his active interest in the work.

On the other hand it was apparent that serum calcium was somewhat dependent upon the net, and whatever the ultimate interpretation of the theory of calcium resorption into the bowel may be this relationship to net is confirmed because Fraction II is related to it in the same degree and way. The level of serum calcium therefore tended to decrease as retention increased in these subjects.

	r	P.E. _r
Serum calcium and calcium balance	-0.44 ± 0.09	
Serum calcium and Fraction II	-0.45 ± 0.09	

The correlation of $+0.83 \pm 0.04$ between serum calcium and fecal calcium was of particular interest and showed that a fair degree of relationship existed between them. It will be recalled that the serum calcium was determined under fasting conditions during the time when the intestinal contents sampled as feces were being formed. Does this finding, then, support the theory of calcium resorption into the main channel of calcium excretion? In this connection it is of interest to refer again to the independence of serum calcium and calcium ingestion and the twenty-four-hour excretion of calcium into the maternal urine.

There was a very mild degree of correlation between the subjects' serum calcium and the stage in pregnancy which they had reached when these tests were made.

	r	P.E. _r
Serum calcium and fecal calcium	+0.83 ± 0.04	
Serum calcium and Fraction I	+0.32 ± 0.11	
Serum calcium and stage in pregnancy	-0.33 ± 0.11	

Urinary Calcium (expressed in milligrams per c.c.).—In pregnancy, urinary calcium is of particular interest because of fetal-maternal relationships. No such correlation as was found between serum calcium and fecal calcium existed for urinary calcium and either fecal calcium or Fraction II. In each instance they were quite indifferently related. The urinary calcium was as independent of the ingestion as was the serum calcium. Likewise the chlorides and calcium were only remotely related.

The urinary calcium per cubic centimeter was somewhat dependent upon the oxygen consumption—a trend not seen in serum calcium. About the same degree of relationship existed between urinary calcium per cubic centimeter and phosphorus per cubic centimeter.

There was the same degree of correlation between urinary calcium per cubic centimeter and the stage in pregnancy as was seen for the latter and serum calcium per cubic centimeter, but they tend to be independent rather than dependent upon each other. This difference in relationship of course would be anticipated as a natural trend in fetal growth, although our subjects did not have a level of calcium ingestion theoretically yielding much surplus for maternal needs and fetal maintenance.

	r	P.E. _r
Urinary calcium per c.c. and fecal calcium	-0.10 ± 0.12	
Urinary calcium per c.c. and Fraction II	+0.17 ± 0.11	
Urinary calcium per c.c. and calcium ingestion	-0.02 ± 0.12	
Urinary calcium per c.c. and urinary chlorides	+0.23 ± 0.11	
Urinary calcium per c.c. and stage in pregnancy	+0.30 ± 0.11	

Fecal Calcium.—In addition to the interesting manner in which the level of fecal calcium indicated the level of serum calcium, it was possible that a species of equilibrium existed between fecal calcium and oxygen consumption, for the level of fecal calcium tended to drop as the oxygen consumption rose. Fecal calcium had some degree of relationship to weight gain and increased as pregnancy progressed.

TABLE I. CALCIUM BALANCES, SERUM CALCIUM, OXYGEN CONSUMPTION AND WEIGHT GAIN DURING PREGNANCY

SUBJECT, AGE, NORMAL WT.	DAYS PREDELIVERY	SERUM Ca, MG. PER C.C.	URINARY Ca, MG. PER C.C.	FECAL Ca, MG. PER C.C.	FOOD Ca, GRAMS PER DAY	Ca BAL. GRAMS PER DAY	OXYGEN CON- SUMPTION	WEIGHT GAIN, POUNDS	URINARY P, MG. PER C.C.	URINARY CHLORIDES, MG. PER C.C.
IIIa 26 yr. 138 lb.	165	0.099	0.120	1.21	1.06	-0.38	190	2.0	0.542	---
	135	0.099	0.096	1.70	1.90	+0.02	196	6.5	0.525	---
	109	0.116	0.088	1.75	1.82	-0.07	193	13.0	0.644	---
	79	0.115	0.194	1.39	1.14	-0.54	206	16.5	0.511	---
	51	0.113	0.200	1.15	1.55	+0.14	218	22.0	0.656	2.92
IIIb 27 yr. 138 yr.	23	0.126	0.091	1.10	1.96	+0.68	230	25.3	0.406	2.87
	196	0.100	0.194	1.90	2.17	+0.01	213	-2.0	0.645	3.46
	168	0.112	0.094	2.04	1.93	-0.30	193	1.0	0.355	2.58
	140	0.094	0.078	1.08	1.31	+0.06	202	5.0	0.105	2.77
	114	0.093	0.101	1.56	2.39	+0.69	184	8.3	0.557	3.11
VI 22 yr. 110 lb.	84	0.098	0.107	1.40	1.33	-0.24	202	10.5	0.258	1.63
	49	0.094	0.101	0.58	1.48	+0.75	218	13.0	0.461	2.67
	160	0.103	0.094	1.51	0.91	-0.78	180	-2.0	0.342	2.32
	132	0.107	0.106	1.30	1.76	+0.27	188	1.3	0.489	3.20
	97	0.097	0.119	0.90	1.26	+0.15	204	8.0	0.217	1.40
II 24 yr. 101 lb.	76	0.090	0.094	1.06	1.59	+0.38	213	13.3	0.560	3.60
	48	0.093	0.169	1.40	1.73	+0.07	222	16.8	0.585	1.40
	216	0.121	0.139	2.30	1.07	-1.49	186	0	0.398	---
	185	0.104	0.125	2.15	1.06	-1.38	179	3.0	0.624	---
	78	0.108	0.168	1.44	1.07	-0.74	206	22.0	0.427	2.02
VII 23 yr. 111 lb.	46	0.086	0.336	0.91	1.86	+0.71	242	27.0	1.226	8.40
	5	0.089	0.733	0.64	1.66	+0.53	274	34.3	1.073	6.65
	216	0.111	0.180	1.65	1.40	-0.44	190	-6.0	0.823	4.09
	156	0.113	0.147	1.32	1.27	-0.27	184	0.8	0.627	2.69
	6	0.102	0.080	1.59	2.08	-0.35	232	24.0	0.716	---
X 31 yr. 144 lb.	209	0.096	0.155	2.11	2.27	-0.12	199	1.0	0.495	3.09
	41	0.100	0.275	1.60	1.27	-0.58	242	28.0	0.784	3.45
	44	0.101	0.122	1.01	2.16	+0.89	231	25.0	0.552	3.46
	9	0.104	0.143	1.14	2.07	+0.67	266	20.5	0.586	3.58
	84	0.112	0.237	1.40	2.08	+0.31	212	16.0	0.550	3.02
VIII 33 yr. 130 lb.	56	0.100	0.250	1.00	1.01	-0.35	204	16.3	0.459	2.14
	27	0.081	0.177	0.83	1.68	+0.57	219	19.5	0.228	2.28
	3	0.080	0.136	0.97	1.88	+0.69	208	18.3	0.447	2.87

considerably. Therefore to get some insight into some points of doubt a partial correlation technique was used in order to see whether a third factor really influenced the result. The following relationships were studied.

Serum Calcium and Balance, Weight Gain Held Constant.—The correlation between the balance (net) and serum calcium was -0.44 ± 0.09 . This was raised to -0.62 ± 0.07 when weight gain was taken into consideration. Apparently this relationship was affected by growth needs. This seems logical and could be said to indicate that the short-period sampling technique employed probably measured the intermittent trends in calcium utilization during pregnancy.

Serum Calcium and Urinary Calcium, Oxygen Consumption Held Constant.—The correlation between serum calcium and urinary calcium was -0.24 ± 0.11 . This was raised to a -0.38 ± 0.10 when the oxygen consumption was held constant. Although neither relationship is close, the basal condition affected it.

Serum Calcium and Fecal Calcium, Oxygen Consumption Held Constant.—The correlation between serum calcium and fecal calcium was $+0.83$ and ± 0.04 . The figure changed only in the second decimal place when oxygen consumption was held constant, indicating that it had little effect upon the original correlation.

INFERENCES

One can infer

1. That calcium may have been transferred from the blood stream into the bowel and that the levels in each were fairly closely related.
2. That the level of calcium in the food had little effect upon the amount of calcium carried in the serum. The net had some effect.
3. That the fraction of calcium possibly available to the fetus was affected by the oxygen consumption of the mother, bearing in mind that this fraction also contains calcium filtered from the maternal system by the kidney.
4. That measuring serum calcium level alone showed little regarding the ingestion level or the level of calcium in the urine during pregnancy.
5. That serum calcium determinations showed less about maternal weight gain during pregnancy than urinary, food or fecal calcium did.
6. That urinary calcium showed more about oxygen consumption than the level in serum, food and feces did.
7. That of the four calcium levels considered—serum, food, urinary, fecal—the fecal level was the most sensitive indicator of weight gain during pregnancy for these subjects, the urinary level being the most sensitive indicator of oxygen consumption.
8. That of the four types of "balance" considered—net, Fraction I, Fraction II, Fraction III—Fraction II predicts weight gain and oxygen consumption equally as well as net, and Fraction I predicts oxygen consumption just slightly better than either of them.

The fecal calcium had almost as clear a relation to weight gain during pregnancy as the balance (net) itself did, although it was independent of the absolute weight of the subject.

	r	P.E. _r
Fecal calcium and oxygen consumption	-0.45 ± 0.09	
Fecal calcium and weight gain	-0.44 ± 0.09	
Fecal calcium and weight	-0.23 ± 0.11	
Fecal calcium and stage in pregnancy	-0.61 ± 0.07	
Calcium balance and stage in pregnancy	+0.60 ± 0.07	
Calcium balance and weight gain	+0.50 ± 0.09	
Calcium balance and weight	+0.54 ± 0.09	

Fraction I and Fraction II Compared.—Fraction I decreases as the oxygen consumption rises ($r = -0.60 \pm 0.07$), Fraction II and oxygen consumption tend to increase synchronously ($r = +0.61 \pm 0.07$). Fraction I decreases somewhat as the weight gain increases ($r = -0.41 \pm 0.09$), while Fraction II increases ($r = +0.55 \pm 0.09$). Fraction I is not closely related to stage in pregnancy ($r = +0.32 \pm 0.11$), Fraction II decreases in size as pregnancy progresses ($r = -0.67 \pm 0.07$) and predicts the net itself quite spectacularly ($r = +0.99 \pm 0.01$).

Apparently the urinary and gastrointestinal systems reacted differently in respect to calcium excretion. The serum calcium alone is somewhat affected by the level of Fraction II ($r = -0.45 \pm 0.09$), the urinary calcium is quite independent of it ($r = +0.17 \pm 0.11$). This finding confirms and is in accord with the relation demonstrated between fecal and serum calcium.

Fraction III.—Fraction III was designed to study ingestion and the calcium filtered by the kidney. It proved to have little relation to serum calcium, oxygen consumption, weight gain or stage in pregnancy. It correlated with the calcium balance well enough to be substituted very grossly for the net itself if fecal output were not known, but it is too easily affected by other elements to be of much value in studying any other phase of metabolism considered here.

	r	P.E. _r
Fraction III and serum calcium	-0.15 ± 0.11	
Fraction III and oxygen consumption	+0.35 ± 0.11	
Fraction III and weight gain	+0.18 ± 0.11	
Fraction III and stage in pregnancy	+0.15 ± 0.11	
Fraction III and calcium balance	+0.70 ± 0.06	

Weight Gain.—It is evident from the preceding discussion that both serum calcium and urinary calcium were poor predictors of weight gain, nor did the levels of ingestion affect the gain very much. The fecal calcium, as was stated above too was somewhat lowered as weight increased, and it was about as good a predictor of gain as the entire balance or Fraction I which indicates the amount possibly available to the fetus.

The weight gain was more closely related to the oxygen consumption ($r = +0.88 \pm 0.03$) than to the absolute weight of the subjects ($r = +0.60 \pm 0.07$).

GENERAL CONSIDERATIONS

In the preceding discussion paired relations were considered, some of which proved to be fairly significant. For several of the pairs, one would suspect that other factors might modify the degree of correlation

cided to inject lipiodol into the uterus to confirm the diagnosis. This was done and we were surprised to find that the lipiodol had easily ascended well into the abdominal cavity showing the fetal sac was connected with the uterine cavity. The patient was readmitted to the hospital Sept. 11, 1936, and after three days of rest and observation a laparotomy was performed. We realized that delivery from below would be impossible because of the long cervix and the large mass to the right blocking the pelvis.

On opening the abdomen a large, gray brown sac was seen, which obviously contained the fetus. The omentum was adherent to the sac over much of its anterior and superior surfaces. These adhesions were partially freed and the sac incised. There was little or no bleeding. The sac wall was friable and tore readily. The macerated nearly full-term fetus was extracted without difficulty. It was then seen that the fetus had been contained in a thin sac which arose from the fundus of the

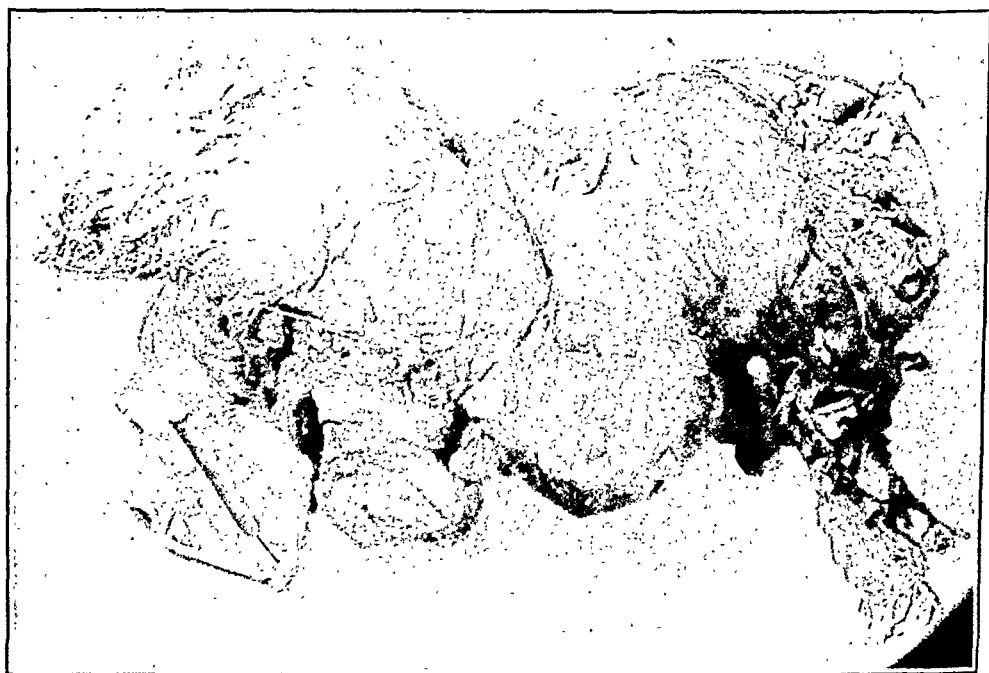


Fig. 1.—View of entire gross specimen.

uterus. The sac was about 2 mm. in thickness and obviously fibrous in character. The placenta was attached to the mucosa of the uterus proper and the inner wall of the sac. Due to the poor condition of the patient a rapid supravaginal hysterectomy was done, the normal looking ovaries were left in situ, thus removing the uterus, sac and placenta in toto. The abdomen was closed in layers. During the operation an intravenous infusion of glucose and saline was given, and the patient left the table in fair condition. Shortly afterward she was transfused with 500 c.c. of whole blood. The patient's condition continued grave for twenty-four hours, and then she rapidly improved. She was discharged from the hospital on her sixteenth post-operative day.

A careful histologic study of the specimen was made. Figs. 1 to 5 illustrate our findings. A block of tissue was taken from the uterus proper, another from the junction of the uterus and the sac and a third block from the sac itself. These sections were studied with hematoxylin eosin and Van Gieson stains. We found an hypertrophied but otherwise normal musculature of the uterus in the first specimen. In the second specimen the transition from the normal musculature to fibrous tissue

Since urinary calcium alone is better related to oxygen consumption than Fraction III and as well related as Fraction I, the level of fecal and urinary calcium alone is a fair indicator of the relation of the total calcium supply of the mother to some body needs and changes during pregnancy. The rate of change in each is of course not clarified enough by this study since it is based on pooled twenty-four-hour sampling.

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A CASE OF FULL-TERM PREGNANCY WITH ACUTE SACCULATION OF THE UTERUS

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PATIENT, Mrs. C. F., twenty-three years of age, colored, was admitted to the Sydenham Hospital Aug. 22, 1936. Her last menstrual period was the first part of October, 1935. There was some spotting in November, 1935. The patient first became ill in the latter part of November, 1935, and was confined to bed with pain in her back and abdomen and continued spotting. In the last three months of her pregnancy she had some left lower quadrant pain and some vomiting. She had received no prenatal care but said that she felt fairly well throughout her pregnancy except as noted. She stated that she had not felt fetal movements for one week prior to admission. She had always been well and had never been operated upon, and considered herself a perfectly normal, healthy individual.

Physical examination revealed a rather poorly nourished, colored female, not acutely ill. Abdominal examination showed an enlargement the size of an eight months' pregnancy; the fetal parts were clearly felt. Her blood pressure was 100/75. The fetus was in breech presentation. No fetal heart could be heard, nor were fetal movements noted. The gravid womb had the typical "dead" sound of a dead fetus. X-ray confirmed the breech presentation and showed overlapping of the fetal skull bones. The Aschheim-Zondek test was negative. The blood Wassermann and Kahn tests were negative. The urine showed a faint trace of albumin but was otherwise negative. The blood count was normal with the exception of a secondary anemia. Vaginal examination revealed an elongated, tightly closed cervix; the presenting part was very high. Three separate attempts were made to induce labor with castor oil, quinine, and pituitrin, with no results. She was discharged from the hospital in fair condition on Sept. 7, 1936, and was told to report to the clinic regularly.

The patient was seen in the clinic on Sept. 10, 1936. The above findings were confirmed and a diagnosis of intraabdominal pregnancy was made. The important points that led to the making of this diagnosis were that the dead fetus seemed to be just under the abdominal wall, and that on bimanual vaginal examination a hard mass about the size of an eight weeks' pregnancy, seemingly an extension of the uterus, was felt to the right with the fetus above and to the left. It was de-

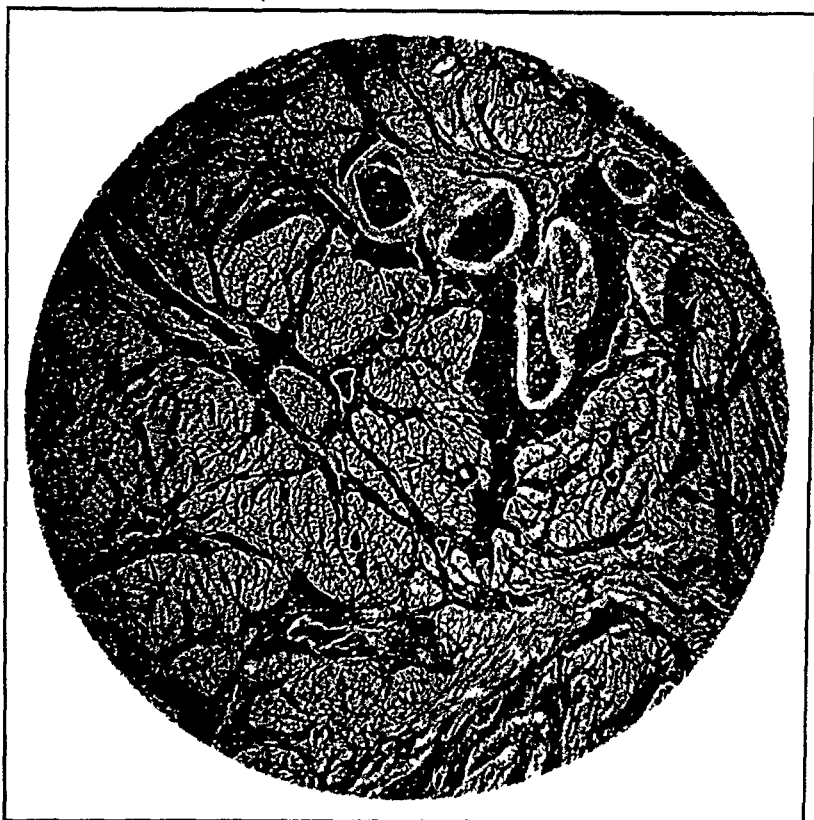


Fig. 3.—Section of uterine wall, showing much glandular tissue. (Van Gieson stain.)

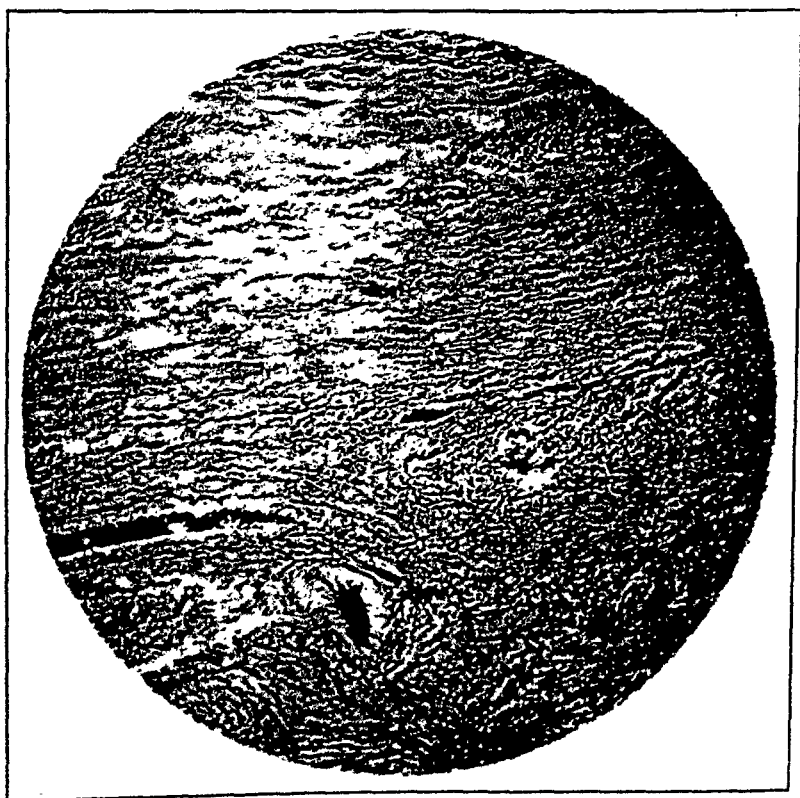


Fig. 4.—Section of the musculo-fibrous junction, Van Gieson stain, showing some muscle fibers and considerable fibrous tissue.

could be seen, and in the third the predominant tissue was fibrous but there were still numerous uterine muscular fibers present.

The sacculation occurred on the fundus of the uterus to the left of the midline and in no way connected with either fallopian tube. The cavity of the sac was connected with the cavity of the uterus by an opening that admitted one finger easily, but no more. The placenta was attached almost entirely to the inner surface of the uterus, whereas the fetal membrane occupied the sacculated portion.

DISCUSSION

It might be well to review in brief the facts of the history and the findings of the physical examination, which suggested to us that this was a case of abdominal pregnancy. We recalled the spotting after the first month of amenorrhea, the acute bed-confining illness in the second or third month of the pregnancy (the sac probably formed at this time); the vomiting and left lower quadrant pain during the last trimester of the pregnancy; the fetal death without even an attempt by the womb



Fig. 2.—Another view of gross specimen.

to empty itself; the very high presenting part and the malposition; the ease with which we could palpate the fetal parts and the tightly closed and uneffaced cervix and the uterus to the right. Any three or four of these might strongly suggest an intraabdominal pregnancy; all of them together made us so sure that something was amiss, that in spite of the negative x-ray findings, it was decided to deliver this patient from above.

Shaw described a condition which he termed "acute sacculation of the uterus." In his case he found a sac coming off the fundus of the uterus, in which a four months' fetus lay. He refers to Döderlein's textbook on *Obstetrics*, in which it is stated that Freund, Schickele, and Hellendall have reported similar cases. All have definite explanations for the phenomenon. The most likely seems the explanation of Shaw himself, who suggests that as a result of failure of fusion of the müllerian ducts, there is some weakness in the uterine musculature.

In our previously reported case of extrauterine pregnancy, we thoroughly reviewed the literature on that subject. At that time no cases corresponding to this one were noted. We have, therefore, reason to believe that this case has its counterpart only in the cases reported by the authors listed above.

Vascularity and cellularity of villi greatly decreased. (C) Sections show a wide layer of muscle tissue in the state of vacuolization and cloudy swelling. Inner surface is covered with necrotic placental tissue. (D) Sections show edematous bundles of smooth muscle fibers. Wall of blood vessels thin and surrounded by a collar of round cells. Here and there the muscle fibers show cloudy swelling and vacuolation. No endometrial lining found. (E) Sections show a wide layer of smooth muscle fibers with thin and wide fibrous septa. The muscle tissue fuses with an overlying layer of partly necrotic or hyaline placental tissue. (F) Sections present a picture identical with "A." (G) Lobules of fat tissue are loosely adherent to underlying structure which presents a picture identical with "F" and "A." The fat tissue is infiltrated with round cells. Above the trabecular layer there is edematous and disintegrating placental tissue. (H) Sections show fibromuscular tissue with muscle tissue predominating and with scattered areas of lymphocytic infiltration.

SUMMARY

Thin part of uterus consists of trabeculae of hyalinized connective tissue interspersed with atrophic muscle fibers, thicker portion of wall consists of degenerated muscle.

CONCLUSION

Because of the predominance of hyalinized connective tissue on one hand and the presence of degenerated muscle on the other, it is reasonable to assume that the uterine wall was structurally defective prior to pregnancy, that the myometrium was inadequately supplied with muscle fibers and that the pregnancy having occurred in a structurally weak uterus was instrumental in the dilatation thinning out and sac-like herniation of uterine wall.

Pathologic Diagnosis: Pregnancy in structurally defective uterus with herniation of uterine wall.

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Cotte, G.: Remote Results in Autogenous Ovarian Grafts With Preservation of the Uterus, Gynec. et obst. 34: 257, 1936.

In a series of ninety-two patients in whom adnexal or ovarian disease existed, the author preserved the uterus and performed autogenous ovarian grafts. Intra-peritoneal sites, preferably the great omentum, were selected for transplants because subcutaneous locations proved less satisfactory and provoked cyst formation.

Activity of the graft most frequently becomes manifest about the third month postoperative. Reestablishment of menstrual function is the certain test of activity of the graft. Although the graft functions as the normal ovary, menopause occurs earlier. In more than half of the patients the periods were regular; in two cases excessive bleeding after a year of normal menstruation necessitated removal of the graft. The reappearance of periods in three patients operated upon after forty years of age is stressed as evidence that age is not an important factor.

Ovarian grafts performed in cases where acute adnexal disease existed were slower in functioning and had a briefer duration than those in which there was chronic adnexal disease.

ARNOLD GOLDBERGER.

Pathologic Report.—(Dr. A. A. Eisenberg).—Specimen measured 23 by 19 cm., opened in operating room. External surface gray brown and had a rough appearance. Scattered throughout the external surface there were several flat elevations ranging in size from 2 to 3 cm. and presenting on section a white, coarse appearance. Over an area measuring 13 by 10 cm., the external surface was covered with omentum. The latter was adherent along the upper border of insertion. Otherwise it was free. The lower end of the specimen, apparently fundus, measured 6 by 3 by 5 cm. The remaining part of specimen was a thin-walled sac, measuring 16 by 16 cm. The width of the wall of the sac varied from 0.04 to 0.02 cm. On section through the wall, the blood vessels were wide open. The greatest part of the cavity was occupied by placental tissue. The amniotic membrane was gray brownish, semitranslucent and

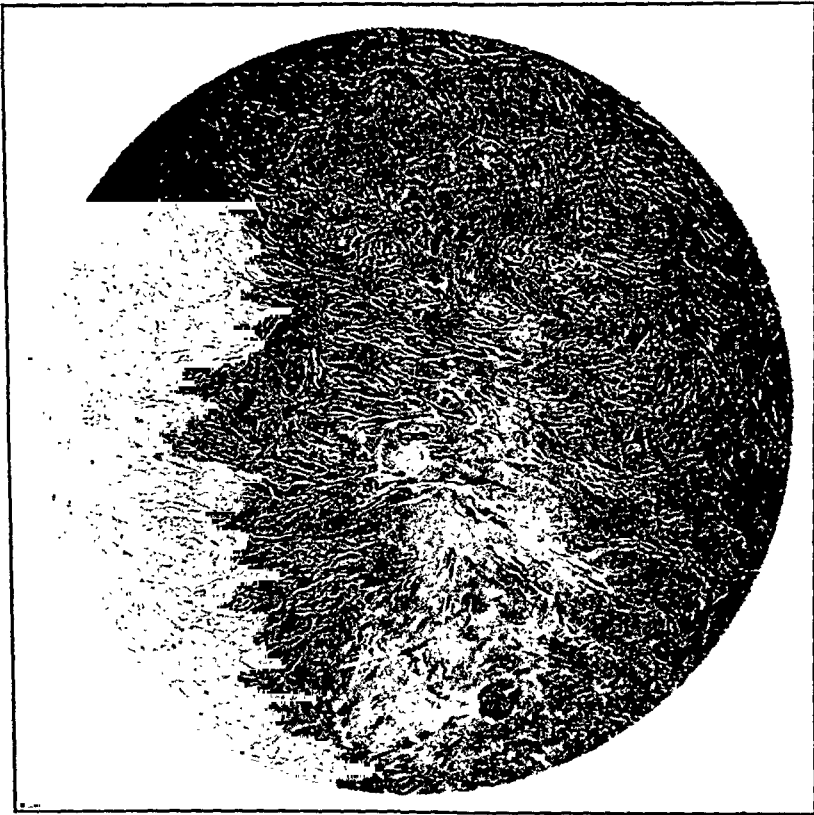


Fig. 5.—Section of the wall of the sac, Van Gieson stain, showing large quantities of fibrous tissue and very few muscle fibers.

measured in its widest diameter 22 cm. The placenta measured in its widest diameter 19 cm. and 14 cm. in its narrowest diameter. On section the placenta was flat and measured from $\frac{1}{2}$ cm. to 1 cm. in thickness. The appearance of the placental tissue was pinkish. To either side of the placenta, the inner surface of the sac had a corrugated or flat nodular appearance and the color varied from gray to green and pink. On section the inner layer was gray brown, the outer layer was gray white. A piece of cord, measuring 24 cm. in length, was inserted eccentrically.

(A) Sections show homogeneous interlacing trabeculi of eosinophile tissue which enclose numerous capillary and sinusoidal vessels. Compressed and atrophic muscle fibers are intermingled with the eosinophile trabeculi; the atrophic muscle fibers usually border on the eosinophile tissue which predominates. (B) Sections show placental tissue resting upon a moderately wide layer of vacuolized muscle tissue. The placental tissue as well as the stroma of villi is here and there hyalinized.

TABLE I. ANALYSIS OF ALL DATA

	NUMBER	PERCENTAGE
Total cases	187	100.0
Pregnant	75	40.0
Nonpregnant	112	60.0
False positives	18	9.5
False negatives	39	21.0
Correct diagnosis by chemical test	130	69.5
Total ovulation tests	69	100.0
Chemical tests agreeing with ovulation tests	50	72.5
False positive chemical tests	7	10.1
False negative chemical tests	12	17.4

It is difficult to explain the discrepancy between our results and those of other investigators on the basis of old reagents, albumin, or reducing materials, all of which are known to decrease the accuracy of the reaction. In this study, reagents were prepared daily, and few of the false positives showed albumin or sugar (Table II). Why this reaction gave such a high number of incorrect results in clinically proved cases of pregnancy cannot be accounted for, at present.

TABLE II. ANALYSIS OF FALSE POSITIVE REACTIONS

Without explanation	13
Albumin	1
Sugar	4
Total	18

Dolff⁶ reported that a positive chemical test could be obtained with prolan in concentrations varying from 50 rat units to as little as 0.8 mouse units. In this study, 4 c.c. of a standardized extract of the gonadotropic factor of the anterior pituitary gland containing 15 rat units per c.c. failed to give a positive test. Antuitrin-S (Parke Davis and Co.) in concentrations varying from 2.5 to 100 rat units likewise failed to give a positive chemical test. The potency of antuitrin-S was demonstrated by the fact that 0.5 c.c., equal to 50 rat units, readily produced ovulation in a rabbit.

The mechanism of the Visseher and Bowman test is believed by some workers^{5, 6} to be in the nature of an oxidation-reduction reaction. Since diabetic urines were found to give false positive reactions, it was decided to determine the effect of various sugars on the chemical test. One to 10 per cent solutions of glucose gave a russet color and a granular precipitate. Considering the possibility that other urinary constituents enter into the reaction, known negative urines were made up to contain glucose in percentages ranging from one to ten. These still showed a negative chemical test, as did lactose and galactose solutions in concentrations of 0.05 to 4 per cent. The presence of a russet color with glucose solutions causes difficulty in interpreting results, but the absence of a

THE CHEMICAL PREGNANCY TEST OF VISSCHER AND BOWMAN

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WITH the advent of the Aschheim-Zondek¹ test and its various modifications, the diagnosis of pregnancy has become more accurate. However, these tests are time consuming and expensive, thereby limiting their routine use.

In 1934, Visscher and Bowman² described a chemical test for the determination of pregnancy. This consisted of adding to 1 c.c. of urine 1 drop of 0.5 per cent hydrogen peroxide, 5 drops of 5 per cent phenylhydrazine hydrochloride, 5 drops of 5 per cent methyl cyanide and 5 drops of concentrated hydrochloric acid. This mixture was heated in a boiling water-bath for twenty-five minutes and the interpretation of the test was made on the color of the solution and the nature of the precipitate present. A russet color and a flocculent precipitate were interpreted as a positive test. A straw-colored solution and the absence or presence of a granular precipitate were considered negative. Visscher and Bowman made a correct diagnosis in 93 per cent of 317 urines from pregnant and nonpregnant women. They believe their findings comparable to results obtained with the rabbit ovulation test³ which has an established accuracy of 95 per cent.⁴ Their technic is simple and inexpensive, and it has the advantage of rendering a diagnosis within half an hour. Menken⁵ in 1934, using the same technic, found, in a small series of cases, that the chemical test agreed for the most part with the clinical findings. Dolff⁶ in 1935, in a series of fifty-four cases which were followed clinically, found that his results closely approximated those of Visscher and Bowman. With the exception of urines containing albumin and large amounts of reducing substances, these workers found the test to be quite reliable as a diagnostic procedure.

The purpose of this work is to attempt to confirm the findings of Visscher and Bowman² and to study the probable mechanism of their reaction. One hundred and eighty-seven specimens of urine from pregnant and nonpregnant patients were tested. Of this series, 118 were followed clinically for a sufficient length of time to establish a diagnosis; 69 of the 187 cases were checked with the rabbit ovulation test (Table I).

A correct diagnosis was made in 69.5 per cent of the total cases studied; 9.5 per cent gave false positive reactions; and 21 per cent were falsely negative in known cases of pregnancy. The chemical test agreed in 72.5 per cent of the 69 ovulation tests and gave 10.1 per cent false positive and 17.4 per cent false negative reactions.

7. The titration method described by Visscher and Bowman in their original article could not be confirmed.

The authors express their gratitude to Dr. C. A. Elden for his cooperation and suggestions in this work and for his help in the preparation of the manuscript.

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RESULTS WITH THE VISSCHER-BOWMAN PREGNANCY TEST

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INVESTIGATORS have again turned to the field of chemistry in their search for a dependable, simple, and quick procedure for the determination of pregnancy. Earlier efforts proved difficult as well as unreliable, and chemical methods were abandoned for the accurate but more expensive and time-consuming biologic tests originally introduced by Aschheim and Zondek and later modified by Friedman. Visscher and Bowman have recently described a chemical test which has considerable promise. Like the biologic methods, it is based upon the presence of the gonadotropic hormone in urine of pregnant women, and, according to Dolff, the chemical reaction taking place in this test depends on the oxidation of the anterior pituitary-like hormone. The procedure is inexpensive, rapid, and simple, and is carried out as follows: To 1 c.c. of urine are added 1 drop of 1 per cent hydrogen peroxide, 5 drops of 1 per cent aqueous solution of phenylhydrazine hydrochloride, 5 drops of 5 per cent aqueous solution of methyl cyanide, and 5 drops of concentrated hydrochloric acid. The mixture is then heated in a boiling water-bath for twenty-five minutes. The test is positive for pregnancy if a russet color develops and a flocculent precipitate appears. A straw color, with or without the presence of a powdery precipitate, indicates a negative reaction. Finer gradations of these reactions were described by Dolff, as follows: strongly positive, dark red brown with a heavy, flocculent precipitate; positive, red brown with a slight, flocculent precipitate; weak positive, or suspected, brown with a light, powdery precipitate; negative, clear yellow with no precipitate. We, also, have observed these graduated readings, and consider them important.

flocculent precipitate indicates that neither glucose nor the other sugars tested are responsible for the characteristic reaction obtained with pregnancy urines.

The question arose as to whether creatine (a known constituent in the urine of many pregnant women) was responsible for the positive chemical reactions obtained. Creatine was therefore added to known negative urines so that each cubic centimeter contained 1 to 2 mg., but no russet color or flocculent precipitate appeared. Histidine is another substance present in varying amounts in urines of pregnant women. Aqueous solutions of *d-l* histidine hydrochloride were employed in concentrations varying from 1 to 7 mg. per c.c. All of these tests gave a negative reaction as manifested by the presence of a straw-colored solution in which a finely granular precipitate was found.

Dilute solutions of albumin gave a dark red solution and a flocculent precipitate which definitely interfered with the interpretation of the reaction. Menken⁵ reported that he had seen a flocculent precipitate in only a few cases and made his diagnosis mainly on the color of the reaction. Analysis of the data here indicates that urines considered positive on the basis of a russet color alone, without the presence of a flocculent precipitate, would be incorrectly reported in 75 per cent of such cases. In definitely positive reactions, a heavy flocculent precipitate was always obtained, and in weaker reactions a granular-flocculent precipitate. Therefore the presence of a flocculent precipitate is definitely necessary before a urine can be called positive by this test.

All attempts to confirm the titration method described by Vissscher and Bowman² gave unsatisfactory results. Since it was practically impossible to read a sharp, definite end point, no correlation could be found between the titration values and the presence or absence of pregnancy.

SUMMARY

1. Of 187 urines examined by the technic of Vissscher and Bowman for the determination of pregnancy, 69.5 per cent agreed with the clinical diagnosis.

2. Approximately 9.5 per cent of the 30.5 per cent of incorrect chemical reactions were false positives and 21 per cent false negatives.

3. The chemical test agreed with the Friedman modification of the Aschheim-Zondek test in 72.5 per cent of the 69 cases.

4. The specificity of this test for anterior pituitary-like substance in the urine of pregnancy, capable of producing ovulation in rabbits, could not be established.

5. A russet color and flocculent precipitate could not be obtained with histidine, creatine, glucose, lactose, or galactose, which indicates that these substances are not responsible for the reaction.

6. A russet color and a flocculent precipitate should be present before a test be considered positive.

fectious processes or postoperative reactions, made up the largest part of this group. The negative reactions (54.8 per cent) were found in afebrile patients. In the known pregnancies studied by us, correct findings were in urines with a specific gravity of 1.015 or higher, while approximately 90 per cent of the incorrect reactions occurred in more dilute urine. Essentially the same was true of urines from patients suspected of pregnancy. This observation we consider highly significant.

CONCLUSIONS

Our results show a higher percentage of error than that recorded by other workers. Elimination of urines of low specific gravity and those containing undesirable catabolic products might better our results. In the suspected pregnancies, where these elements do not come into play, our findings were 87.6 per cent correct, the highest percentage of accuracy we found in any group. Contrasted with this, the fewest number of correct results (54.8 per cent) occurred in urines of nonpregnant *febrile* patients.

We must conclude from our results, as well as from the results of other investigators, that the Visscher-Bowman test for pregnancy is, as yet, not sufficiently reliable to supplant the biologic methods now in use. A modification of the technique, aiming at the elimination of the sources of error, may ultimately yield a very useful diagnostic method.

SUMMARY

1. Three hundred ninety-five urines were tested by the Visscher-Bowman method for the determination of pregnancy. Correct reactions were obtained in 84.8 per cent of 250 known pregnancies, 87.6 per cent of 65 suspected pregnancies, and 54.8 per cent of 62 nonpregnancies.

2. Urines of low specific gravity or containing unusual amounts of catabolic reducing agents tend to give false reactions.

3. The test in its present form is subject to too high a percentage of error to replace the Friedman and Aschheim-Zondek tests.

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Visscher and Bowman tested 317 known pregnancies in this manner and obtained a correct reaction in 295, or 93 per cent. They also compared their test with the Aschheim-Zondek test in 40 clinically suspected pregnancies. The two methods corresponded in 33 instances and conflicted in 7. Of the latter, 3 gave positive chemical but negative Aschheim-Zondek tests; one nonpregnant patient known to have a uterine fibroid gave a negative chemical and a positive Aschheim-Zondek test; and 3 cases were not clinically controlled.

In Dolff's report on 83 patients, correct tests were recorded in 96 per cent of known pregnancies, 95 per cent of early pregnancies, and 82 per cent of ectopic pregnancies. In nonpregnant patients he obtained a negative reaction in urines of low specific gravity and a positive reaction in those of high concentration, but his figures for this group were not reported. He interpreted these false positive reactions as being due to an increase of catabolic products in the urine.

In a very small series of cases Menken reported a close correlation of clinical and chemical findings in both late and early pregnancy. In more recent observations, Dodds found the test correct in 90 of 100 pregnancies. Her report also included 80 nonpregnant gynecologic patients, 89 per cent of whom gave a negative test. The author recorded the diagnosis of the patients with false positive reactions but failed to cite their temperatures.

We have made Visscher-Bowman tests on 395 urines. Of 250 patients clinically proved pregnant, 212, or 84.8 per cent showed a positive reaction. We studied 65 patients in whom pregnancy was suspected by both Friedman and Visscher-Bowman tests. Of 41 patients giving positive Friedman tests, we obtained 36 positive and 5 negative Visscher-Bowman reactions; and in 24 patients giving negative Friedman tests we found 21 negative and 3 positive chemical reactions, a correlation of 87.6 per cent. A clinical follow-up of the latter group showed the Friedman tests to have been 100 per cent correct.

Since Dolff found that false positive reactions were likely to occur in urines high in catabolic products, we investigated the urines from 62 nonpregnant gynecologic patients. False positive reactions were obtained in 45.2 per cent of cases. Patients with fever, due either to in-

TABLE I

	LATE PREGNANCIES (CLINICAL)	PER CENT CORRECT	EARLY PREGNANCIES (CLINICAL)	PER CENT CORRECT	SUSPECTED PREGNANCY, CHECKED WITH A-Z OR FRIEDMAN, AND CLIN- ICAL FOLLOW-UP	PER CENT CORRECT	NONPREGNANCIES	PER CENT CORRECT
Visscher-Bowman	317	93.0			37*	92.0		
Dolff	54	96.0	18	95				
Menken	8	88.0	4	100			11	100.0
Dodds	100	90.0					80	89.0
Dunn	250	84.8			65	87.6	62	54.8

*Three of Visscher-Bowman's 40 cases were not clinically controlled, and therefore have not been included in this table.

pregnant patients and 6.6 per cent in the postpartum cases, while 81.6 per cent of the men and 66.6 per cent of the nonpregnant women showed false positive tests for pregnancy (based on skin reactions one hour after the injection). Furthermore, intradermal injections of phenolized normal saline gave definite erythematous reactions in 8.8 per cent of our subjects one-half hour after the injections and in 5.4 per cent at one hour.

TABLE I. RESULTS OF CUTANEOUS TESTS FOR PREGNANCY

CLASSIFICATION	NUMBER EXAMINED*	POSITIVE CUTANEOUS REACTIONS				PERCENTAGE OF ERROR			
		ANTUITRIN-S (A.P.L.H., P.D. & CO.) ‡		A. P. L. H. § (PLACENTAL)		ANTUITRIN-S (A.P.L.H., P.D. & CO.) ‡		A. P. L. H. § (PLACENTAL)	
		½ HOUR	1 HOUR	½ HOUR	1 HOUR	½ HOUR	1 HOUR	½ HOUR	1 HOUR
Postpartum	15	2	1	5	3	13.3†	6.6†	33.3†	20.0†
Pregnant	48	12	10	18	17	25.0	20.8	37.5	35.4
Men	38	15	7	24	17	60.5	81.6	36.8	55.3
Nonpregnant Women	12	7	8	10	10	58.3	66.6	83.3	83.3

*Saline controls yielding positive reactions at one-half hour, 10; at one hour, 6.

†Based on the assumption that these should yield negative cutaneous reactions.

‡A. P. L. H., P. D. & Co., Anterior pituitary-like hormone, Parke, Davis & Co.

§A. P. L. H., Anterior pituitary-like hormone extracted from placental tissue.

CONCLUSIONS

In our hands the anterior pituitary-like hormone (antuitrin-S) cutaneous test for pregnancy was found to be entirely unreliable.

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Rivoir, J.: Vaginal Secretion as a Cause of Primary and Recurring Cystitis, Monatschr. f. Geburtsh. u. Gynäk. 105: 344, 1937.

As emphasized by Rivoir, infection of the urethra plays an important rôle in inflammation of the bladder. The urethra is infected not only by the gonococcus but also by the staphylococcus, streptococcus, colon bacillus, etc. The author believes that about 70 per cent of women who have a chronic infection of the genitalia also suffer from a nonspecific infection of the urethra. Cystoscopic examination in these women demonstrates a trigonitis which, in the chronic cases, produces no noteworthy symptoms. Hence the author favors treatment of all vaginal discharges as a prophylactic measure against nonspecific infections of the urethra and trigonum.

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ANTUITRIN-S CUTANEOUS TEST FOR THE DIAGNOSIS OF PREGNANCY

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NUMEROUS attempts have been made to develop procedures for the early diagnosis of pregnancy which are simpler and more rapid than the highly accurate Aschheim-Zondek and Friedman biologic tests. Recently the intradermal injection of anterior pituitary-like hormone has been revived by Gilfillen and Gregg¹ as a "new, rapid, economical test for pregnancy and certain gynecologic conditions."

Most of the previous reports in the literature concerning the value of the test have been unfavorable.² Since the recent encouraging report by Gilfillen and Gregg is so at variance with the previous literature, we have carried out a series of tests to determine the value of the procedure.

This study was carried out on 113 individuals. Fifty were normal men and nonpregnant women; 48 were known cases of pregnancy of two or more months' duration and fifteen were from one to nine days postpartum.

Each subject received three intradermal injections; two of which were different preparations of the hormone, namely (1) antuitrin-S which is an extract of pregnancy urine prepared by Parke, Davis & Co., and (2) an anterior pituitary-like hormone extracted from placental tissue.* These have apparently identical physiologic effects but are derived from different sources. The third injection was a control consisting of normal saline with 0.5 phenol. Each injection amounted to two minims. In order to check the possibility of differences in reaction to preparations of separate dates, antuitrin-S from three lots and placental anterior pituitary-like hormone from two lots of manufacture were used in this study.

The skin reactions were noted at intervals of one-half, one, and twenty-four hours following the injections. Results of the first two readings are shown in Table I. At the last reading, practically all subjects showed an area of erythema at the site of both the antuitrin-S and placental anterior pituitary-like hormone injections.

From the results it is evident that there exists a marked discrepancy between the skin reactions and the clinical diagnoses. The errors of the test consist in both false positive and false negative reactions. Using antuitrin-S, 20.8 per cent false negative results were obtained in our

*The author wishes to express his appreciation for this material to Dr. R. W. Whitehead, Department of Physiology and Pharmacology, University of Colorado School of Medicine.

pregnancy present. Eight patients gave a doubtful reaction while 76 gave no reaction at all. In the pregnancy cases, therefore, the test was only 68 per cent accurate. Two of the postpartum patients were tested within one hour after delivery and both gave no skin reaction within the next hour; both, however, showed strongly positive reactions five to six hours later. A number of the positive skin tests lost their erythema within a few hours, but most of them remained red for one or two days. Almost all of the patients with positive skin tests complained of pain at the site of injection although there were no infections in the entire series. Of the nonpregnant patients, all showed definite skin reactions; some more positive (extensive) than others.

The second hormonal product studied was anterior pituitary luteum (Ayerst), an anterior pituitary-like hormone derived from the placenta. This substance was alcohol free. It was used in only six patients all of whom were definitely pregnant. The results are tabulated in Table II.

TABLE II

TYPE OF CASE	TOTAL	SKIN REACTION		
		POSITIVE	NEGATIVE	DOUBTFUL
Prenatal (pregnant)	6	2	3	1

In this small series, this product produced results only 50 per cent accurate, and its use was discontinued.

The third and final product studied was progesterin (Upjohn) a corpus luteum extract from fresh glands containing corpus luteum hormone which plays such an important rôle in the physiology of pregnancy and menstruation. This was used in 29 cases with the following results, Table III.

TABLE III

TYPE OF CASE	TOTAL	SKIN REACTION		
		POSITIVE	NEGATIVE	DOUBTFUL
Prenatal (pregnant)	10	9	0	1
Medical (nonpregnant)	15	14	1	0
Newborn (one to ten days)	4	4	0	0
Total number of cases tested	29			

An analysis of this series shows that 98 per cent of all cases, including the pregnant women, produced a positive skin reaction rendering this test definitely inaccurate.

We must conclude, therefore, that the use of anterior pituitary-like hormone injected intradermally in the manner suggested by Gilfillen and Gregg, and scientifically controlled, in a series of 198 cases, did not provide an accurate or reliable skin test for pregnancy.

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1882 GRAND CONCOURSE
1229 CLAY AVENUE

SKIN TESTS FOR PREGNANCY

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GILFILLIN and Gregg, in the September, 1936, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, presented a series of cases in which they found that "antuitrin-S, when injected intradermally, provides a reliable, simple, quick, economical, and accurate guide in the diagnosis of pregnancy." The theory propounded was that, since there is an anterior pituitary-like substance in the urine of pregnant women, pregnant women should not be sensitive to its intradermal application, and that nonpregnant women should show a dermal reaction to its injection. In other words, a positive skin reaction indicates the absence of pregnancy. The absence of a skin reaction indicates that pregnancy is present.

This pregnancy test was apparently first proposed by Porges and Pollatschek¹ of Vienna. It was subsequently investigated by Alfred Deutsch² in Europe and by Hyman Strauss³ in this country. Both these workers found the test to be quite unreliable.

In order to verify the findings of Gilfillin and Gregg and to corroborate the above-mentioned theory, the following tests were done on a series of 198 cases on the Obstetric Service of Dr. Meyer Rosensohn, at The Bronx Hospital. Three different laboratory hormonal products were used. In all cases 0.2 c.c. was used intradermally on one arm while a like amount of sterile saline solution was used as a control on the other arm. In order to avoid pseudoreactions due to dermatographia, infection, chemical irritation, such as alcohol, etc., only saline solution was used to cleanse the skin fifteen minutes before the test. Likewise, no product with an alcoholic base was used.

The first hormonal product used was antuitrin-S (Parke, Davis & Co.), an anterior pituitary-like substance derived from the urine of pregnant women. This was injected intradermally in 163 cases with the following results (Table I):

TABLE I

TYPE OF CASE	TOTAL	SKIN REACTION		
		POSITIVE	NEGATIVE	DOUBTFUL
Prenatal (pregnant)	112	28	76	8
Medical (nonpregnant)	22	21	1	0
Postpartum (1 hour to 9 days)	21	21	0	0
Pediatrics (2 to 10 years)	8	8	0	0
Total number of cases tested	163			

An analysis of this series shows that of 112 definitely pregnant women, 28 gave a positive skin reaction, falsely indicating that there was no

Thus, from the preliminary work of Hines and Brown, it appeared that their "cold test" might serve to differentiate hypertension due to parenchymatous nephritis from that due to vascular disease. Further, an exaggerated response in an individual with normal blood pressure seemed to suggest strongly a hypertensive diathesis (latent hypertension).

Dieckmann and Michel, and Randall and Murray were quick to see the possibilities of such a test as applied to the toxemias of pregnancy. In a preliminary paper, Randall and Murray² suggested that the test might reveal impending toxemia before the appearance of the classical signs. Dieckmann and Michel³ also in a preliminary report, placed more emphasis upon the potential value of the test in prognosis and in differentiating between the acute toxemias and "chronic nephritis" by which they apparently mean both primary hypertension and chronic parenchymatous nephritis.

If there is practical value in the test, it would seem to us to lie in the aid it might give in prognosis and differential diagnosis as pointed out by Dieckmann and Michel. If it is true that the "cold test" will distinguish between primary and secondary hypertension, and will reveal latent hypertensive vascular disease; and if it is also true that responses to the test are not altered by normal pregnancy, obviously the "cold test" should be invaluable in the differential diagnosis of hypertension during pregnancy.

For two years we have used the "cold test" repeatedly upon a considerable number of both normal and toxemic patients during the course of pregnancy and in the puerperium. The technique which we have used in performing the test does not differ materially from that described by Hines and Brown. The patient assumes a comfortable reclining position, and the blood pressure is taken at intervals of a few minutes until a basal level is reached. This usually requires from ten to forty minutes. The opposite hand is then placed in an arm bath filled with ice water at 4° C. for two minutes. The blood pressure is recorded each thirty seconds during the period of the immersion and subsequently until it has returned approximately to the basal level. The maximum rise in systolic and diastolic pressure is taken as the response to the test.

The rise in blood pressure is apparently in response to the pain induced by the ice water. From experimenting upon ourselves and others, we have made several observations which have some bearing upon the interpretation of results. First, the subjective pain experienced varies to a considerable extent in the same individual when the test is repeated at different times although the conditions of the test remain constant. Second, the maximum pain occurs after some twenty-five to thirty seconds of immersion, and the hand subsequently becomes relatively numb. This observation is to be correlated with the fact that a maximum response in blood pressure is almost always

A STUDY OF THE "COLD TEST" IN NORMAL AND IN TOXEMIC PREGNANCY

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THERE is urgent need for some test or system of diagnostic procedures which would make possible the immediate and accurate classification of patients with hypertension, albuminuria and edema during pregnancy. Recognition of this need has led to the proposal of a number of tests, the purposes of which have been to distinguish between preeclampsia and eclampsia on the one hand, and vascular or renal disease independent of pregnancy, on the other. The common orthodox procedures are applications of tests used by internists to measure renal function. Among the more valuable of these are concentration and dilution of urine, phthalein excretion, blood chemistry, and urea clearance. If proper allowance is made for the peculiarities of the physiologic state of pregnancy (such as the tendency to retain water) these tests may be made to yield valuable information. However, they are of little or no positive value in the differentiation of essential hypertension, mild parenchymatous nephritis without significantly impaired renal function and preeclampsia. Further, they do not solve the problem of whether the increases which we so commonly see in the blood pressures (often accompanied by urine changes) of known hypertensives and nephritics during the last trimester of pregnancy are exacerbations of these diseases or the superimposition of preeclampsia.

Recently the "cold test" as described by Hines and Brown¹ has attracted considerable attention. These authors studied the response of the basal blood pressure to a standard cold stimulus from immersing the hand in ice water. They found that a characteristic exaggeration in the response to the test as measured by the rise in systolic and diastolic blood pressures was shown by 98 per cent of their patients with primary hypertension. Patients with hypertension due to nephritis failed to show this exaggerated response to the test.

Further, in a group of subjects with normal blood pressures, some 20 per cent showed an exaggerated response to the test. Of these individuals with normal blood pressures but with exaggerated response to the cold stimulus, the immediate family history was positive for hypertension or death from apoplexy in at least 75 per cent of the cases.

systolic response to the test on at least one occasion was greater than 20 mm. (3) The response exceeded 30 mm. systolic on one or more occasions in 8 patients. In only one of these latter cases was there a family history of hypertension.

Response to the "Cold Test" During Toxemic Pregnancy.—Five normal patients whose family histories were negative for hypertensive disease and whose past histories revealed no nephritis were followed from early pregnancy. Routine examinations included blood pressure, urinalysis, and weight, and in addition the "cold test" was performed at intervals of about six weeks on each patient throughout pregnancy. Each of these patients developed toxemia late in pregnancy. The "cold test" was performed eighteen times antepartum upon these 5 patients, and in only two instances were systolic responses greater than 20 mm. Hg obtained. One of these was obtained in a patient at the first test early in pregnancy when the blood pressure was normal. The responses of this same patient later in pregnancy were subsequently less than 20 mm. systolic even when the blood pressure was elevated due to toxemia.

Of 17 other patients who developed toxemia during pregnancy but whose blood pressures were normal both before the onset of toxemia and again postpartum, 11 showed systolic responses of 20 to 40 mm. Hg at the time of the toxemia. Thus, in 17 patients who may be fairly said to have had uncomplicated toxemias of pregnancy, there was no uniformity of response to the test.

Response to the "Cold Test" During Pregnancy of Patients With Essential Hypertension.—There were 14 patients upon whom "cold tests" were performed whose past histories, courses during pregnancy and follow-up examination for at least six months postpartum justified a diagnosis of essential hypertension. Only 6 of them showed systolic responses greater than 20 mm. Hg.

Pickering and Kissin⁴ applied the "cold test" to a series of non-pregnant patients. Their results failed to confirm those of Hines and Brown that an exaggerated response to the test is characteristic of patients with latent or developed essential hypertension. Observations of our own upon a limited series of nonpregnant subjects are in accord with the findings of Pickering and Kissin.

CONCLUSIONS

The results of our own study on normal and toxemic pregnant patients fail to support the suggestion that the test might reveal impending toxemia. Nor do we find the test of practical value in the differential diagnosis of pregnancy toxemias. Although the number of patients in our groups is too small to exclude a general relationship between the magnitude of the response to the test and essential hypertension or other forms of hypertension during pregnancy, the marked variations in response in

elicited by immersion of the hand for thirty seconds. The responses of the same individual to the test when it is repeated at intervals of several days are usually of the same general pattern although differences of 20 mm. Hg systolic in the maximum response are not infrequent. In our hands, the systolic response is more consistent than the diastolic when determined by the usual clinical sphygmomanometer and stethoscope.

In the original article of Hines and Brown, the average systolic and diastolic responses of the "normal" group of subjects were 8.62 and 8.14 mm. Hg. These authors regarded 15 mm. Hg as the maximum normal systolic response. Randall and Murray allowed 20 mm. Hg as a maximum normal systolic response. We have been able to confirm the observation that the response to the test is minimized or abolished by sedatives and anesthesia.

Response to the "Cold Test" During the Course of Normal Pregnancy.—The "cold test" was performed at intervals of from four to six weeks throughout pregnancy and puerperium upon 34 normal patients. In all, 159 observations were made upon this group of patients. None of them developed systolic blood pressures of 140 mm. Hg or more, or albuminuria or significant edema. The average rise of systolic and diastolic blood pressures in the different periods of pregnancy and puerperium in response to the "cold test" is shown in Table I. The individual variation in response to the cold fluctuated from three instances in which syncope developed with accompanying fall in blood pressure, to one instance in which the systolic rise was 62 mm. Hg. It will be seen from the table that although there is perhaps a slight tendency toward increase in response as pregnancy advances, such increase is probably not significant.

TABLE I. THE AVERAGE RISE IN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE IN RESPONSE TO THE "COLD TEST" IN THE DIFFERENT PERIODS OF PREGNANCY AND IN THE PUERPERIUM. THE TABLE IS CONSTRUCTED FROM 159 OBSERVATIONS UPON 34 PATIENTS

WEEKS DURATION	PREGNANCY				PUERPERIUM	
	8-16	17-24	25-32	33-40	1-2	6+
Number of observations	22	32	33	32	26	14
Av. rise systolic blood pressure	14.86	13.70	19.40	17.00	13.40	19.10
Av. rise diastolic blood pressure	10.63	11.06	9.20	10.90	12.90	18.00

Further examination of the results of the test in these 34 normal patients permits a number of interesting observations. (1) There were 4 subjects in whom the systolic response was always greater than 20 mm. Hg. Four or more tests at intervals of more than four weeks were done in each instance. The family histories in 3 of these patients were negative for hypertensive disease. We had the opportunity to personally check the blood pressures in the immediate families of two. (2) There were 16 patients or exactly half of the group in whom the

Estrogenic hormone was determined by the Fluhmann method.⁶ This test is based on the stimulation of the atrophied vaginal mucosa of the test animal (mouse). Whereas earlier tests utilized this principle by observing changes in the vaginal mucosa by smears, Fluhmann's procedure is dependent on "the histologic demonstration of certain changes in the vaginal mucosa of recently spayed mice which precede cornification, the most important of which is the formation of tall columnar cells secreting mucus (mucification)." Although this change was formerly thought to be a specific effect of a corpus luteum hormone, more recent investigation has demonstrated conclusively that mucification is an effect of estrin, and that the production of this change by corpus luteum extracts is due to the presence of small amounts of estrogenic hormone in these preparations. Thus mucification is recognized now as an estrogenic hormone response.

METHOD

The animals used were young adult female mice, which had been spayed nine days prior to the onset of the test. For convenience to the operator the mice were spayed on Monday morning and were available for injection on the following Wednesday morning.

For this problem the test materials were blood samples taken from mother and child at the time of parturition. The mother's blood was obtained by venipuncture. The fetal blood was obtained by "milking" the cord before expression of the placenta. These blood samples were always obtained within the twenty-four hours immediately prior to the onset of the test. The samples were kept sterile; the clear serum separated by centrifugation and kept in the ice box. The time element is important in view of the possible variation of hormone content due to standing several days.

The previously prepared mice were injected three times daily; 0.5 c.c. at 9:00 A.M., 1:00 P.M., and 5:00 P.M., for three consecutive days. On the morning of the fourth day, the mice were killed and after abdominal incision and splitting the symphysis, the vagina was dissected free and fixed in formalin. The individual specimens were mounted in celloidin, sectioned at two or three levels and stained with hemotoxylin and eosin.

Because of the biologic variation in response to any one dosage, three or four mice were used for each determination. Thus this technique adhered closely to that originally published by Fluhmann.

The Fluhmann tests were performed using varying concentrations of maternal and fetal blood serums. In the earlier tests in the series, full strength serums were injected. The results revealed such a high concentration of estrogenic hormone, however, that subsequently both maternal and fetal serums were diluted with normal salt solution. Dilutions of 1:2, 1:4, 1:8, 1:16 and 1:20 were used. The maternal and fetal serums of any one set of injections were always of the same dilution.

RESULT

As the concentration of estrogenic hormone in the tested serums became less, due to dilution, the degree of response became progressively lessened also. Thus, with the more dilute serums the type response was such as to allow for fairly delicate discrimination.

different patients of each clinical group, as well as considerable differences in the response of the same patient at different times, would exclude any value for the test in differential diagnosis for any individual case.

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THE PRESENCE OF ESTROGENIC HORMONES IN MATERNAL AND FETAL CIRCULATION

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THE problem of passage of substances through the placenta has been subjected to extensive investigation since the demonstration of the absence of anastomoses between maternal and fetal circulations.

Rupp¹ and Schlossmann² in authoritative monographs, discuss the permeability of the placenta to carbohydrates, proteins, lipoids, salts, hormones, vitamins, antibodies and antigens. Brandstrup³ also notes that through the work of Slemmons, Von Oettingen, Hellmuth, Runge and others, we now have quantitative data on various salts, glucose, urea, uric acid, creatine, creatinine, amino acids, proteins, lipoids and lactic acid.

The phase of this problem which has interested us most is the question concerning the presence of hormones in the fetal circulation. In a previous paper⁴ the bibliography concerning the permeability of the placenta to various hormones was presented. Snyder, Snyder and Hoskins, Schlossmann and others have discussed the problem of transmission of adrenalin, insulin, posterior lobe of the pituitary and parathyroid extract. Soule⁴ discussed the transmission of anterior pituitary or anterior pituitary-like hormones (Prolan B).

The literature concerning the presence of estrogenic hormone in the fetal circulation is meager. Schlossmann, quoting Courrier and von Loewe, concludes that female sex hormone (folliculin) is demonstrated in fetal blood. Skowron and Skarzynski,⁵ working with rabbits, conclude that the placenta permits follicular hormone to pass through.

The most expedient method for the study of the interchange of substances between the mother and fetus is a comparative analysis of the maternal and fetal blood at the time of parturition. The approach to the problem in this laboratory is based on the simultaneous determinations of the presence of estrogenic hormone in human maternal and fetal blood.

dominal incision reaching from just below the xyphoid to just above the symphysis pubis. The abdomen is closed behind the uterus by through-and-through sutures. The uterus is then opened and the child delivered. The uterus and adnexa are allowed to remain on the abdominal wall for twenty to thirty days when they are replaced by a second laparotomy or the "réintégration" of Portes.

Döderlein¹ points out that this technique was suggested by Gottschalk in 1909 in the *Berliner Gesellschaft* and again in 1911 in Munich at the Gynaekologen-Kongress. It seems he did not use the operation, however. After Portes' original report in 1924 the operation was used widely in the Latin countries and later in Austria and Germany. In 1926 G. A. Wagner reported a small series of cases with good results, and in 1931 L. Kraul² reported one case with good result. His method differs in that he delivered the fundus of the uterus only so far as to allow the adnexa to remain within the peritoneal cavity. In this way he avoided closure of the tubes by granulation tissue incident to the weeks of extraperitonization and also the necessity of a second operation to replace the uterus. He sutured the unopened uterus laterally to the edges of the recti muscles. Here it remained and as involution took place, the uterus spontaneously sunk back into the peritoneal cavity. The result was a uterus fixed to the anterior abdominal wall after healing.

Kraul's method has the advantages mentioned of avoiding a second operation and closure of the tubes but it defeats the chief purpose of Portes' technique, namely removal of the uterus and adnexa from the peritoneal cavity until danger of spreading infection is past. Certain difficulties in Portes' technique should be pointed out, however. The acute anterior flexion of the uterus in lifting it through the abdominal wall and the necessary delay in delivering the child until the abdominal wall is closed may give rise to uterine apoplexy with resultant death of the child. The danger of peritonitis when the uterus is replaced is negligible if smears and cultures are taken before laparotomy. Poor union of the uterine wall is a more serious consideration in cases of union by second intention which is to be expected in such infected cases as demand this radical treatment.

It would seem to me that the bad points of Portes' technique are more than offset by the following advantages: A woman frankly infected who cannot be delivered from below may still be saved by cesarean section with very little danger of infection so long as the uterus and adnexa remain outside the peritoneal cavity during the first twenty to thirty days. The operation requires only a few minutes and may be used in patients who could not survive a longer more complicated operative procedure. Closure of the tubes may be largely overcome by the use of rubber tissue instead of moist gauze dressings. In this way the uterus and reproductive function may be preserved while minimizing the danger from infection while delivering through the abdomen.

These three case reports illustrate the use of Portes' technique where the patient was admitted late in labor, in extremis, frankly infected, and where delivery was impossible from below. Two are cases of deformity due to osteomalacia, one is a chondrodystrophic dwarf. In the first case wet gauze dressings were used. The tubes were completely closed by adhesions and granulation tissue. In the third case rubber protective was used and no gauze allowed to touch the uterus or tubes. Although the patient died after four days, there was no sign of granulation tissue formation, and it seems probable that this use of protective would decrease the incidence of closure of the fimbriated ends.

From the standpoint of puerperal infection the results in Cases 1 and 3 were satisfactory. In Case 1, there was an elevation of temperature from the fourth to the eleventh day, but the patient was feeling well, taking a general diet, the abdomen was soft and there were no signs of peritonitis, in spite of the fact that there was a drainage of huge quantities of pus from the uterus. After the eleventh day there

The degree of mucification as determined by the Fluhmann test was always the same in corresponding maternal and fetal serums in all dilutions.

The observation is most interesting when one recalls that most hormones are *not* found in similar concentrations on the two sides of the placental barrier.

CONCLUSION

1. Estrogenic hormones are present in equal concentration in both maternal and fetal circulations.

2. The presence of estrogenic hormone in marked concentration in the fetal circulation is consistent with the clinical observance of enlarged breasts and bloody vaginal discharge in newborn infants.

3. Considering that there is no evidence that the fetus produces an excess of estrogenic hormone, we may assume that the placenta is permeable to estrogenic hormone.

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THE VALUE OF CESAREAN SECTION WITH PORTES' TECHNIQUE IN THE PRESENCE OF INFECTION, WITH REPORT OF THREE CASES

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THE treatment of frankly infected patients in whom delivery from below is either impossible or necessitates a destructive operation on a living child, has long been a matter of discussion. Classical section followed by supravaginal amputation of the uterus is usually considered the safest, but in a young woman, perhaps in her first pregnancy, it is far from ideal. Also the surgical risk to an exhausted patient is considerable. Transperitoneal or extraperitoneal section does not remove the source of infection, namely the uterus, and is not free from danger of subsequent peritonitis. Also almost the same surgical risk is encountered as with the amputation of the uterus.

In 1908 Sellheim suggested using a uterine-abdominal fistula in these cases. This allowed free drainage of the uterus and the abdominal cavity was protected by suturing the edges of the open uterus into the abdominal incision. A second laparotomy was necessary to return the uterus into the abdominal cavity. This operation seems to have been widely used in Germany. In 1924 L. Portes first suggested and used the "exteriorisation" of the uterus in cases of infection. The technique consists briefly in delivering the entire uterus and adnexa intact through an ab-

in the hospital. On the fifth day the uterus began to discharge foul pus which was very profuse, saturating the entire bed. The white blood count was 28,000, with 94 per cent polymorphonuclears. The uterine sutures sloughed out, leaving a gaping incision which, however, provided wide and safe drainage outside the abdomen, which remained soft and undistended. Dakin's solution was used to irrigate and dress the uterus. A general diet was taken and the condition of the woman was excellent.

Involution took place normally and by the nineteenth day culture showed only a few staphylococci present. Five days later, under local anesthesia the uterus was sutured and replaced into the abdomen. A mercurochrome cigaret drain was left in the uterus which was later removed through the vagina. The abdominal wall was closed in layers and the rest of the stay in the hospital was uneventful. Both tubes were closed by adhesions at the fimbriated ends and further pregnancy was not probable. Sterilization, however, was not done on account of the refusal of the husband and woman herself. The patient was discharged from the hospital Feb. 27, 1934, and seen May 7 in the dispensary when she was in excellent condition.

CASE 2.—(13537) Mrs. C. Y. S., admitted to the Hunan-Yale Hospital Feb. 5, 1934. The woman had been in labor for four days, 3 of which she had spent at home under the care of a native midwife. Twenty-four hours before admission she had been taken to a Chinese hospital where large doses of pituitrin had been injected.

The patient was a twenty-year-old primigravida. Past history could not be obtained other than that she had been blind for some years.

Physical examination showed a woman acutely ill, pale, sweating, pulse weak, 140 per minute, temperature 35.5° C., blood pressure not obtainable. Both eyes were blind and scars of old trachoma evident. The lungs were clear, heart sounds faint but no murmurs heard. The abdomen was enlarged to the size of a term pregnancy but the uterus was tetanically contracted over the fetus, making it difficult to palpate the fetal parts. The child presented by vertex, which markedly overrode the symphysis. No fetal heart tones were heard. No presenting part could be reached by the examining finger in the rectum and a foul meconium-stained fluid was being passed from the vagina.

The most striking point in the physical examination was the small stature of the woman whose height measured approximately 40 inches. The spine was twisted with a marked lumbar lordosis which had caused the promontory of the sacrum to descend downward and forward to the level of the symphysis, thus doubling the sacrum on itself. This gave a greatly decreased anteroposterior diameter to the sacrum with a diagonal conjugate also decreased to 6 cm. The sacral promontory lay directly behind the symphysis. The external pelvic measurements were, spines 23, crests 25, trochanters 25, Baudeloque's 16, and tuber ischii 7.5 cm.

The blood count was R.B.C., 4,780,000; W.B.C., 13,450; Hb 106 per cent; polymorphonuclears, 81 per cent. No urine was obtained on catheterization.

Although there was no history obtainable of a decrease in stature, the bony deformity was characteristic of osteomalacia.

The woman was at once given supportive treatment, heat, intravenous glucose, and saline hypodermoclysis. Using ether anesthesia she was prepared for laparotomy. A midline incision was made from the xyphoid to 15 cm. above the symphysis. The bladder was dark, hemorrhagic, and the lower uterine segment was of paper thickness, in places gangrenous. Extreme care was necessary in delivering the unopened uterus in order not to rupture the lower segment during the flexion. On this account the upper end of the abdominal incision was not sutured until after delivery of the child. Large gauze packs and towels were used to protect the upper abdomen from contamination by the uterine contents as well as the routine packing off of the lower incision. The tightly contracted uterus which outlined the body of the fetus like a

was no further elevation of temperature and the recovery was uneventful. In Case 3, the patient died on the fourth day, but up to this time showed no evidence of peritonitis or elevation in temperature.

All three patients were extremely bad surgical risks. In Case 1, which survived, the pulse was 120, blood pressure 104/60, temperature 37.2° C. In Case 2 the pulse was 140, blood pressure could not be obtained, temperature 35.5° C., and in Case 3 the pulse was 120, blood pressure 68/42, temperature 37.2° C. It was felt in each case that amputation of the uterus would not have been survived, while Portes offered a rapid delivery with little additional shock. In each case the condition after operation was no worse than when the patient went onto the table. In addition, as Cases 1 and 3 illustrate, infection was adequately cared for.

CASE 1.—(13406) Mrs. T. P. S., admitted to the Hunan-Yale Hospital Jan. 12, 1934, after being in labor eighteen hours. She was delivered of a living child in this hospital four years ago by cesarean section and warned that spontaneous delivery would be impossible. In spite of this she remained at home attended by a Chinese midwife until after the rupture of the membranes.

Past history was unimportant but for the fact that she did not walk until two years of age. There were no serious illnesses or accidents. Menstrual history was regular, onset at seventeen years, last period in April, 1933.

Physical examination showed a woman pale, sweating, cold, exhausted. Height was 132 cm., weight 97 pounds, temperature 37.2° C., pulse 120, blood pressure 104/60. Head and chest were normal. Abdomen was enlarged to the size of a term pregnancy. The fetus presented by vertex, no fetal heart heard. The head was not engaged and definite over-riding at the symphysis was evident. The pelvis measured: spines 20.5, crests 21, trochanters 24.5, Baudeloque's 16, tuber ischii 5 cm. The urine showed 2-plus albumin, red blood cells, and white blood cells. The red blood count was 4,100,000, white blood was 43,300, Hb 91 per cent.

X-ray of the pelvis showed diagonal twisting of the bones with extreme scoliosis of the lumbar spine. The sacrum was displaced to the right, the superior strait was triangular and irregular in shape, with the sacral promontory at the level of the symphysis but to the right of the midline. The diagonal conjugate measured 7 cm. The pubic arch was very narrow which further decreased the available space for delivery from below. Engagement in the superior strait was prevented both by the size and shape of the inlet.

The uterine contractions were every three to five minutes and forceful. Immediate delivery was necessary to prevent rupture of the uterus through the old scar. The outlet contraction was too great to permit of any destructive operation from below and the patient's condition forbade any prolonged surgery, as supravaginal amputation of the uterus after section.

Portes' section was done under ether anesthesia. The abdomen was opened by a long incision from just below the xyphoid to just above the symphysis. The skin was protected with towels and the uterus delivered intact. The abdomen was rapidly closed by through-and-through silkworm-gut sutures above and below the uterus, and protected with more thick gauze pads and towels to prevent contamination from the uterine contents. The fundus was incised and a dead macerated full-term fetus delivered. The placenta was expressed and the uterine incision closed in two layers, first interrupted, the second continuous catgut. The uterus was dressed with moist gauze, dry towels, and a tight abdominal binder applied.

The pulse remained between 120 and 130 during the operation and the patient was sent to her room in good condition. Voiding was spontaneous. Daily dressings with moist saline gauze were applied to the uterus. On the second day the temperature rose to 37° C., pulse 80. There was a further elevation of temperature on the fourth day to 37.8° C. and it continued between 37° and 38.6° C. until the eleventh day when it fell to normal and showed no further elevation during the stay

136 as the patient was returned to her room. Digitalis and ephedrine were given and fluids by vein and subcutaneously, as well as by rectum.

A few hours after operation the temperature rose to 38.8° C. and the pulse to 150, but the next day the temperature was 37.2° C., pulse 120. Fluids were taken well and there was no distention. The second day the dressings were changed. The uterus was clean and no bleeding. On the fourth day the general condition was worse, the temperature was 37° C., respiration was shallow, and the pulse weak, 130 per minute. Involution had begun and the abdomen showed no evidence of peritonitis. In spite of intravenous glucose, digitalis, and general supportive treatment, the patient died four days after delivery of cardiac failure. The hemoglobin at this time was 82 per cent. X-ray of the pelvis showed an anteroposterior contraction with the sacral promontory almost touching the symphysis. X-ray of the child showed normal bony development.

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TISSUE LOSS FROM THE ENDOMETRIUM DURING MENSTRUATION

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HERETOFORE, the description of the changes in the endometrium which characterize the normal menstrual cycle in the human female has been inadequate, in as much as the reason for the death and the dissolution of the cells in the endometrium which results in macroscopic tissue loss, has not been explained.

The observations reported here are based on the first experiment in an investigation which is intended to justify the following conclusion, namely: during the functional stage, the internal economy of the epithelial cells in the endometrium is so altered by the accumulation, within the cell, of the elements of the secretion to be elaborated, that a return to their former state after the stimulus to the formation of secretion has been withdrawn is impossible. Therefore when the stimulus from progestin disappears with the normal degeneration of the corpus luteum at the end of the cycle, these functioning cells die, and dissolution of the cells with tissue loss results.

The development of the endometrium in two monkeys was artificially augmented by the administration of estrone and progestin. Each animal received simultaneously a hypodermic dose of 1 mg. of estrone in oil daily for seven days followed by a hypodermic dose of four rabbit units of progestin daily for five days. A hysterectomy was performed on animal "A" on the day following the last dose, and on animal "B," on the fifth day following the last dose of progestin. The uterus in each

glove, was opened at the fundus in order to avoid the gangrenous lower segment. The child was grasped by the feet and peeled out of the uterus. It was full term, stillborn, and macerated. The placenta was removed and the uterus wiped clean of membranes. The uterus was rapidly sutured in two layers and all dressings removed and the gloves changed. With fresh instruments the abdominal wall was now closed by through-and-through silkworm-gut sutures, both above and below the uterus which was allowed to remain on the surface. The uterus and adnexa were covered by rubber tissue and wet gauze dressings.

The operation lasted twenty minutes and the pulse remained 140 throughout, was small but regular. Fluids were continued with small amounts of ephedrine and digitalis given during the next ten hours. Transfusion was not possible on account of lack of donors, and the patient died ten hours after operation of cardiac failure.

The child weighed 5 pounds. The head measured S.O.B. 9 cm., Bip. 9.5 cm., O.F. 11 cm., O.M. 10.5 cm.

CASE 3.—(13756) Mrs. H. L. S., a primigravida, was admitted to the Hunan-Yale Hospital March 13, 1934, after being in labor for four days. She had been attended by several midwives and the membranes had been ruptured for two days. She could give little past history other than that she had always been small. She was employed as a monkey trainer in a Chinese circus. Her husband was of normal height and physical development. No other members of her family were said to be unusual in any way.

Physical examination showed a woman 132 cm. in height, heavy muscular development, but the bony conformation of a typical chondrodystrophic dwarf. The head was markedly brachycephalic with prominent forehead and saddle nose, the arms and legs were short with great bowing of the tibia.

The patient was exhausted. Labor pains were almost continuous. The temperature was 37.2° C., pulse weak, small, 120 per minute, blood pressure 68/42. Head, heart, and lungs were essentially negative. The abdomen was tense, the uterus tetanically contracted with the fundus lying under the diaphragm on account of the short torso. The child presented by vertex and was estimated at 7 pounds. No fetal heart was heard. The pelvis measured: spines 21, crests 23, trochanters 29, Baudeloque's 14.5, and tuber ischii 6.5 cm. Rectal examination showed the membranes ruptured but only the finger tip could be inserted between the symphysis and the sacral promontory, which lay directly behind the symphysis. The R.B.C. was 3,540,000; Hb, 75 per cent; W.B.C., 24,700; polymorphonuclears, 94 per cent. Urine showed a one-plus albumin with granular casts.

Delivery from below was, of course, impossible with the diagonal conjugate of less than 2 cm. The patient was frankly infected and so poor an operative risk that amputation of the uterus after section was not to be considered. Therefore Portes' technique was decided upon as offering the least surgical shock and at the same time taking care of the infection. Under ether anesthesia the abdomen was opened from 6 cm. below the xyphoid to just above the symphysis. The uterus was found tightly contracted over the fetus and was delivered intact. A contraction ring was found about the neck of the child with the head fixed below the ring. The abdomen was rapidly closed above and below the uterus by through-and-through silkworm-gut sutures and protected by towels and gauze from contamination. The uterus was incised in the midline and it was necessary to carry the incision downward through the contraction ring before it was possible to free the head. The child was full term, macerated, stillborn, but showed no evidence of chondrodystrophy. The placenta was removed and the uterus closed in two layers. The tubes were excised by wedge-shaped incisions and the distal ends buried in the folds of the broad ligament. The uterus was then protected by rubber tissue and dressed with warm moist gauze. The operation required thirty-five minutes in all, and the pulse was



Fig. 3.

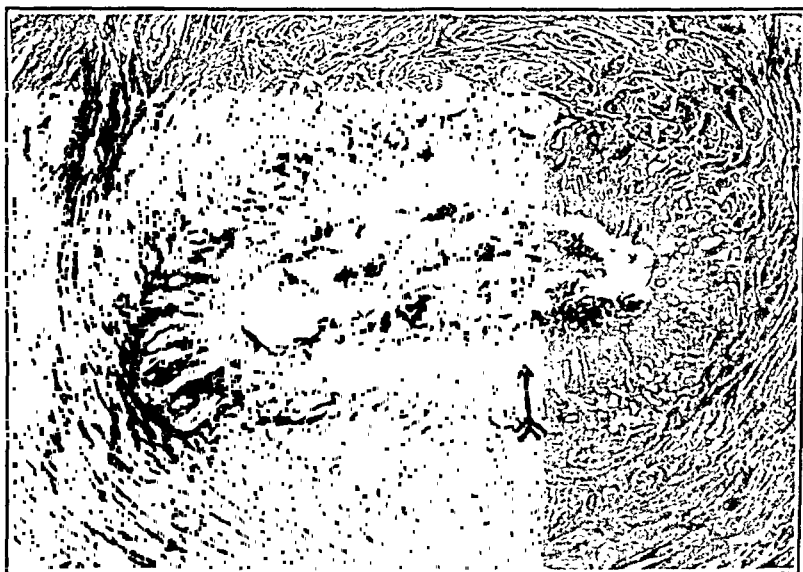


Fig. 4.—The arrow marks the position of the section shown in Fig. 9.



Fig. 5.—The arrow marks the position of the section shown in Fig. 8.

case was manipulated during the operation by grasping the uterine ligaments and the organ was immediately transferred to the fixing fluid.

The photographs shown in Figs. 1, 2, and 3, are of sections from the uterus of animal "A." Fig. 1 represents a cross-section of the uterus from a position close

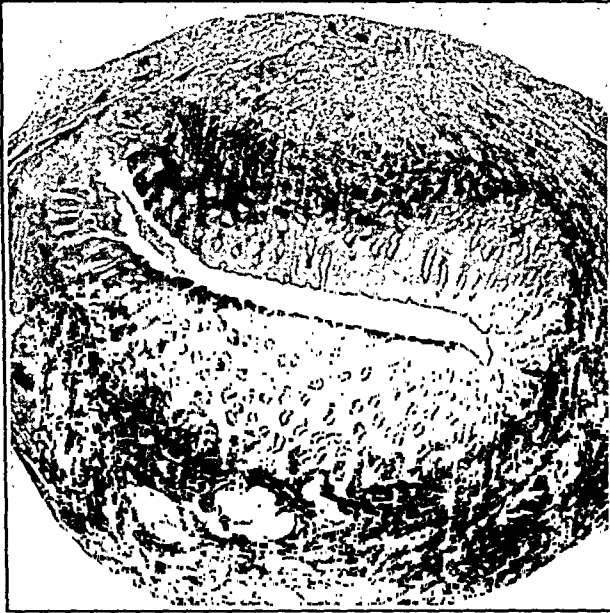


Fig. 1.

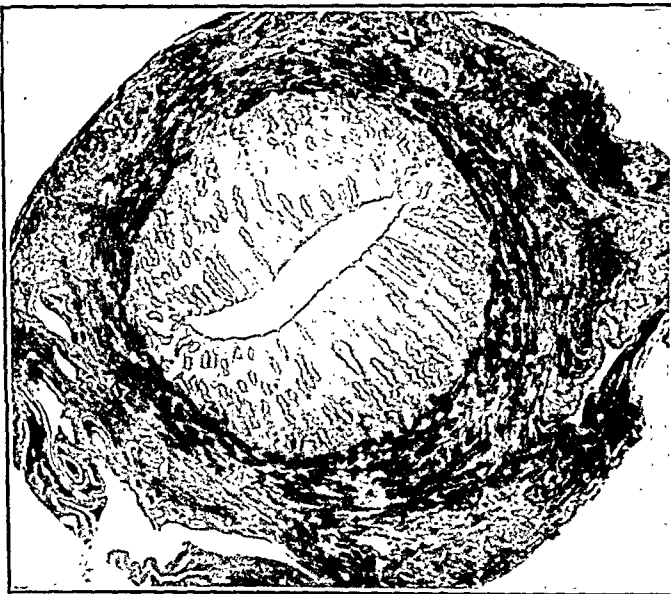


Fig. 2.

to the fundus, and accordingly most of the glands in this photograph are shown in cross-section. Fig. 2 is a photograph of a section taken 4.5 mm. lower in the uterus than Fig. 1, and Fig. 3 is from a section 4.5 mm. lower than Fig. 2. These photographs show clearly that the endometrium in this uterus was in a well-developed functional stage and that it had remained intact because the epithelial lining of the lumen of the uterus was uninterrupted throughout.

plete dissolution, although hemorrhage into the stroma surrounding these glands is not a marked feature. Fig. 9 is a photomicrograph showing marked degeneration in the epithelium of the glands at the position marked in Fig. 4.

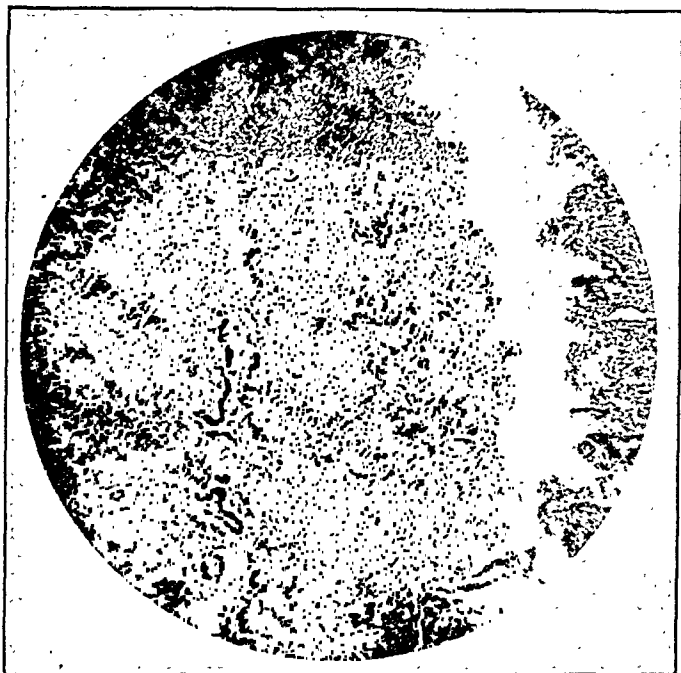


Fig. 8.—Epithelial and stromal cells in the area have completely disappeared. ($\times 250$.)

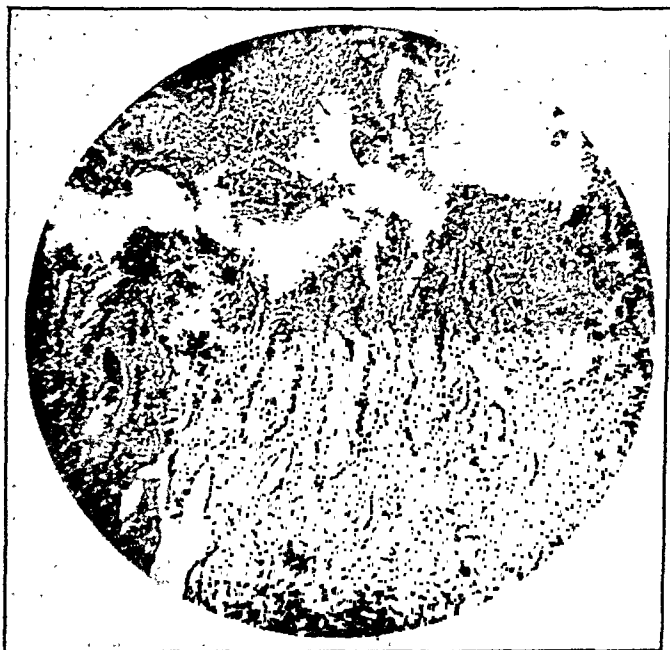


Fig. 9.—Glands along the line of separation in which epithelium is undergoing dissolution. ($\times 250$.)

The central degenerating mass in Fig. 5 is again a complete cast of the original lumen of the uterus. The epithelium which originally surrounded the lumen of the uterus is still recognizable in certain areas as is shown by higher magnification in the center of Fig. 8. While free red blood cells are very numerous in the degenerating mass shown in the center of Fig. 5 there is very little hemorrhage into

The photographs shown in Figs. 4, 5, and 6 were taken from sections of the uterus of animal "B." These photographs show the endometrium as it appears during the process of cellular dissolution and tissue loss after progestin therapy had been discontinued for a period of five days. In Fig. 4 the major portion of the outline of the original lumen of the uterus can be seen in the center of the mass of de-

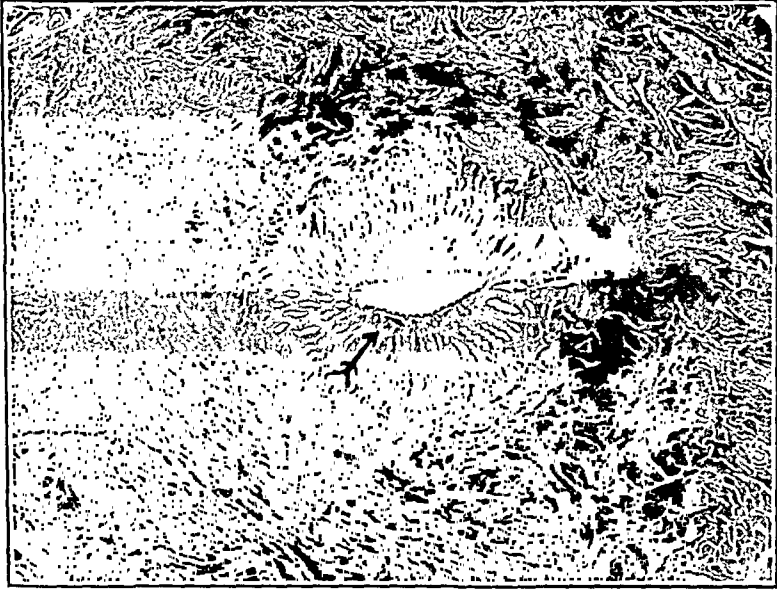


Fig. 6.—The arrow marks the position of the section shown in Fig. 7.



Fig. 7.—Tissues beginning to lose definite outlines in area with extravasation of blood. ($\times 250$.)

generating tissue occupying the newly formed cavity. Dissolution of the epithelial and the stroma cells in this central mass is very complete. In some areas in this degenerating mass the outline of a gland can be recognized but individual cells in the epithelium of these glands cannot be made out. The epithelium of the glands in the superficial area surrounding the new cavity also shows evidence of fairly com-

PREGNANCY IN LYMPHOPATHIA VENEREA, COMPLICATED BY ESTHIOMENE AND RECTAL STRICTURE

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THE Frei reaction is generally accepted as the definite criterion of existing or past infection with the filtrable virus of lymphopathia venerea. A positive reaction depends upon sensitization of tissues to the virus or its by-products. While generally regarded as a localized disease, there are investigators^{1, 2} who, on the basis of experimental and clinical findings, view this entity as a generalized infection with local manifestations at the portal of entry. The results of numerous Frei tests show that in the female, stricture of the rectum and esthiomene or elephantiasis of the vulva usually result from invasion of this virus. Stricture of the rectum is the common manifestation of the disease, Lichtenstein finding esthiomene in only six of 58 cases.³

In the rather voluminous literature dealing with various aspects of this condition the effect of the disease on fecundity and pregnancy has been almost entirely neglected. Wilson⁴ in 1930 reported a number of cases of granuloma inguinale associated with pregnancy. One of the patients also had an elephantiasis of the vulva, but no Frei test, which might have established a diagnosis of lymphopathia venerea, was performed. The same objection must be raised in the case report of Das⁵ describing elephantiasis of the vulva associated with pregnancy, because again no Frei test was done. Recently Gaines and McDowell⁶ described a case of rectal stricture and pregnancy, but again no mention of a Frei test is made. We wish to report a case of lymphopathia venerea with the clinical manifestations of elephantiasis of the vulva and stricture of the rectum with a positive Frei reaction, and to emphasize certain interesting laboratory findings, which may have differential value, if found to exist in all patients suffering from this condition.

CASE REPORT

M. J., thirty-four-year-old negro female, was first seen in the Out-Patient Department of the John Gaston Hospital on April 6, 1926. A diagnosis of chronic salpingitis was made at this time. Due to hemolysis the blood Wassermann was not determined. She next visited the clinic in October, 1927, with the same complaints. The blood Wassermann on this occasion was four-plus. A course of antisyphilitic therapy was instituted, but in May, 1928, the Wassermann was still positive. When seen again in November, 1929, she complained of arthritis in the left knee, but a cervical smear was negative for gonococci. She was now placed on a course of mercury, which was followed rather irregularly until August, 1930. She reappeared in the clinic in February, 1936, and the blood Kahn was now negative. An hypertrophy on the vulva was noted for the first time. On Aug. 28, 1936, she was admitted to the Gynecology Service of the John Gaston Hospital for study of the genital lesion.

The growth on the genitals was first noted three years ago. Redness, tenderness, or acute pain was never present. The swelling has progressively increased in size with definite increase in rate of growth during the past year.

the stroma where the endometrium is still intact. This observation lends support to a speculation that the hemorrhage which occurs during menstruation may be secondary to the death and dissolution of the tissues.

Fig. 6 is a photograph of a section close to the internal os from the same uterus showing very superficial dissolution in the endometrium. The epithelial lining of the lumen in this section is still intact, the epithelial cells of the glands in the degenerating area are quite indistinct and there is a very limited amount of free blood in the area.

CONCLUSIONS

The dissolution of the epithelial cells in the superficial glands of the endometrium in animal "B" is similar to the dissolution of the functioning epithelial cells which we have observed in the glands of the endometrium in the human female following a similar course of treatment with estrone and progestin. Dissolution of epithelial cells in the normal endometrial cycle, only occurs in the epithelium of the glands which have been stimulated to a full functional stage, and then only when the stimulus to function has been withdrawn. Tissue loss from the endometrium during normal menstruation is limited to the epithelium of the glands which have been fully activated by progestin and to the stroma which supports those glands.

The authors are indebted to the Connaught Laboratories for permission to carry out this work and also for gratuitously supplying the estrone which was used. Grateful appreciation is also extended to Professor W. A. Scott for his helpful interest.

We are indebted to the Banting Research Foundation for a grant to one of us (M. W.).

Golub, L. J., and Shelanski, H. A.: Silver Picrate Treatment of Vaginal Trichomoniasis, *J. Lab. & Clin. Med.* 22: 1155, 1937.

These authors have treated 25 patients having *T. vaginalis* with a 1 per cent dispersion of silver picrate in kaolin applied to the vagina with an occluding insufflator; this treatment was followed by a course of six suppositories each containing 2 gr. of silver picrate—one inserted every night starting one day after the insufflation. The patient then returned in one week for another course of insufflation followed by the above suppository treatments. Two such courses of treatment were the usual routine, but in some cases more treatments were required. After each menstrual period, patients were reexamined and the treatment repeated if necessary. The cervical mucous plug must be removed to prevent reinfection. For this purpose a colloidal aluminum hydroxide gel plus kaolin was used; this was followed by cleansing the cervix and vagina with sterile water, the latter being less irritating than green soap. Intercourse, douches and tub baths are to be avoided; hygienic measures are also important.

Methods of transmission are discussed, including the presence of *T. vaginalis* in prostatic fluid, which was responsible for recurrence of symptoms in three cases.

W. B. SERBIN.

Pathologic Report.—(Fig. 2.) A biopsy was taken from the tumor of the labium majus. The section is covered by squamous epithelium which was pigmented, thickened, and slightly edematous. The stroma was markedly thickened, edematous, and consisted of dense fibrous tissue. Numerous dilated lymphatics and thickened blood vessels surrounded by focal collections of lymphocytes and plasma cells were present.

Course in Hospital.—During the eleven-day period of observation in the hospital, the patient ran a rather uneventful course. Temperature, pulse, and respirations were normal. However, the diarrhea persisted, the patient having 2 to 5 loose stools daily. She was discharged to the Obstetrical Clinic on Sept. 9, 1936. Since the submission of this paper the patient has delivered a normal child. She is now receiving antisyphilitic treatment without any amelioration of the local findings. The child has been tested with six different known Frei antigens at various times with negative results. This is contrary to European findings.



Fig. 2.



Fig. 3.

Fig. 2.—Biopsy of lesion on left labium majus showing edema, fibrosis and perivascular round cell infiltration. $\times 70$.

Fig. 3.—A portion of section shown in Fig. 2, demonstrating the same findings under higher magnification. $\times 200$.

DISCUSSION

Notwithstanding the syphilitic background, we feel that the virus of lymphopathia venerea and not the *Treponema pallidum* is the etiologic agent in the elephantiasis of the vulva and the stricture of the rectum. The simultaneous occurrence of syphilis and lymphopathia venerea is a common finding as first pointed out by Coutts and Bianchi;⁷ moreover these clinical conditions commonly occur in nonsyphilitic patients and do not occur in syphilitic patients unless the Frei test is positive. The development of the lesions during the period of antisyphilitic treatment and the negative Wassermann reaction also favor the same etiology. The history of inguinal lymphadenitis in the husband preceding the development of the lesions in our patient suggests the source of the infection.

Menstruation began at fifteen years of age, has been regular and of a twenty-eight-day cycle and lasting three days. Occasionally dysmenorrhea was present. The last period began June 15, 1936, this being the first occasion on which she has ever missed a period.

The patient was married for five years. No previous pregnancies. Husband had a bilateral inguinal adenopathy four years ago. He has not consented to the performance of a Frei test upon himself. Apparently transmission of the virus to the patient occurred at this time, the husband being the source of the infection. For the past eight months she has had a vaginal discharge. Diarrhea has been present for the past two months with 4 to 5 loose stools daily, but without gross pus or blood.

Physical examination revealed a well-developed and nourished colored female not acutely ill. Blood pressure 120/80. Oral hygiene was very poor. The vulva pre-



Fig. 1.—Photograph of genitalia showing elephantiasis of left labium majus.

sented a large mass the size of a grapefruit involving the left labium majus. It was firm, not tender, and of a pinkish brown mottled color (Fig. 1). The cervix was short, soft, and discolored. The uterus was enlarged to the size of a two to three months' pregnancy, symmetrical and soft. The appendages were not identified. Rectal examination revealed an annular stricture, tender to pressure, and would not admit the tip of the examining finger when forced.

Laboratory Findings.—R.B.C., 3,400,000; Hg, 11 gm. per cent; W.B.C., 8,600. Differential: Filamented polymorphonuclears 63 per cent, nonfilamented polymorphonuclears 10 per cent, lymphocytes 25 per cent, large mononuclears 2 per cent; blood Kahn negative. Urine negative. Aschheim-Zondek positive. Frei test 2-, 3-, and 4-plus using seven different antigens. Sedimentation time 30 mm./10 minutes. Blood chemistry: Total protein 9.9 gm. per 100 c.c. plasma; albumin 2.9 gm., globulin 6.5 gm., fibrinogen 0.5 gm., nonprotein nitrogen 17 gm.

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DYSTOCIA DUE TO FETAL TERATOMA

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A LESS commonly encountered cause of dystocia is that due to fetal sacral teratoma. The standard texts mention this congenital anomaly as a potential cause of obstruction but give little or no space to its discussion. DeLee (sixth edition)¹ does not refer to it. Davis² mentions it briefly. Williams³ states, "exceptionally, teratomatous tumors about the perineum and sacrum may offer a serious obstacle." Curtis⁴ quoting Piper says, "cystic tumors should be punctured—solid tumors call for version or embryotomy."

A review of the literature discloses occasional reporting. Saxtorph,⁵ 1775, and Veling,⁶ 1846, report individual cases. In 1867 the first comprehensive review was done by Molk who reported 107 cases. Coudère⁷ in 1890 reviewed 29 cases. Hohl collected 40 cases; Brown, 79 cases. In the past twenty years only isolated cases have been reported: Spitzer⁸ in 1933; Kovats⁹ 1934; Brenner¹⁰ 1935.

The etiology of sacral teratoma is not known, but the blastomere theory of Bonnet, Marchand, and Robert Meyer is the most acceptable one.

The incidence of this tumor as reported by Colbert in 1893 was 1 in 34,082 births; Spitzer in 1932 reported 1 case in 20,042 births. There are no quoted figures as to the incidence causing dystocia, but they are undoubtedly much higher.

In all the reported cases this tumor was never diagnosed antepartum. There have been observed two concomitant findings. The majority of cases have an accompanying hydramnios and by far a great number have premature labors. The size of the mass per se does not inconvenience the patient.

The presentation is preponderantly by the vertex. In Molk's series of 107 cases 100 per cent were vertex. Coudère reports 25 vertex, 3 shoulder, and 1 breech presentation.

The labor records of these cases are for the most part facsimiles of one another. The usual story is that of a normal progressing labor. The head is delivered, but it is during the delivery of the trunk that the obstruction occurs. After vain attempts at extraction have failed, the possibility of this complication is considered and is usually verified by whole hand vaginal examination. A mass is felt impacted in the superior strait.

The treatment varies with the type of teratoma present. The cystic ones can be ruptured, thus relieving the obstruction. The solid tumors cause more trouble. Some

The positive results obtained with seven different Frei antigens is conclusive proof that the lesions are due to lymphopathia venerea. It is generally accepted that a positive Frei reaction with a reliable antigen and proper interpretation is as specific as any immunologic test in the realm of medicine. Bacon⁸ after reviewing the literature on Frei reactions concludes that it is 96.7 per cent diagnostic. We have obtained a positive Frei reaction twenty-four years after the occurrence of bilateral inguinal adenitis. Our antigen is made either from pus or from infected tissue. The original technic of Frei is followed with the exception that the antigen made from infected tissue is allowed to remain in the ice box for several weeks before it is used. Experience has taught that the antigen is not active before this period of time, probably due to absorption of the virus by the tissue. As our criteria of strength of reaction we have followed the classification of Strauss and Howard⁹ except that we have added a fourth class, i.e., four-plus, when the reaction proceeds to necrosis. Readings are made at the end of forty-eight and ninety-six hours, using a micrometer rule for measuring the actual depth and size of the reaction.

The close association of rectal stricture with lymphopathia venerea has been so often and thoroughly commented upon that further discussion is unnecessary.

Esthiomene is the less common clinical manifestation of the disease. The type of lesion depends upon the direction of lymphatic drainage from the site of the initial lesion. Drainage to the inguinal glands results in esthiomene, while drainage to the glands of Gerota results in rectal stricture. The generally accepted concept of the pathologic basis of esthiomene is lymph stasis following lymphatic obstruction, but Dorne and Zakon¹⁰ incriminate the action of the virus on the affected tissues. They also maintain that the virus is active even in the tertiary stage of the disease.

The effect of the virus on fecundity and pregnancy has received but scant attention by workers in this field. Dick¹¹ states that women in the later stages of lymphopathia venerea are usually sterile. The exact mechanism by which sterility is brought about is apparently not definitely known. Some investigators maintain that the virus acts upon the entire generative system, but substantiating proof in the form of gross or microscopic studies is not offered.

Williams and Gutman¹² have recently called attention to two laboratory findings which may have differential value. They found that there is a rapid sedimentation time of the erythrocytes and a reversal of the normal albumin-globulin ration in the blood serum. In the above case the reversal was almost $2\frac{1}{2}$ to 1, and it is to be noted there was no edema. We have found in a series of cases to be published later that the above phenomena occur in practically all patients. We have found the fibrinogen content of the blood serum to be uniformly normal, thus confirming the findings of Williams and Gutman. The exact mechanism of these chemical changes is not definitely known, but these workers attribute them to the same factors operative in other chronic infections such as kala-azar and leprosy, and in certain neoplastic diseases such as multiple myeloma.

SUMMARY

1. The first proved case of lymphopathia venerea with esthiomene associated with pregnancy is presented.
2. The patient presented rectal stricture and esthiomene, the usual manifestations of this disease.
3. The Frei test was positive, and reversal of the albumin-globulin ratio and rapid sedimentation rate, both constant findings in lymphopathia venerea, were present in this case.

Pathologic Report: The full-term female fetus with a crown-heel measurement of 50 cm. had normal head, trunk and extremities. Protruding from the perineal region between the rectum and coccyx was a globular mass measuring 16 cm. in diameter, entirely covered by skin. The rectum was present as a dilated orifice on the anterior surface. Some portions of the mass were cystic and others solid, the cystic portions containing clear, serous, straw-colored fluid and being lined with smooth, glistening membrane. The solid portion consisted of lobulated, soft, pinkish gray tissue which was somewhat friable and containing small spicules of calcium.

All internal organs were normal. The lungs were atelectatic except along the anterior margins where they were pink and containing air.

Microscopic Diagnosis.—Sections through various parts of the tumor showed many types of embryonal and adult tissue. Some postmortem degeneration was evident. The stroma consisted chiefly of a mesenchymatous myxoid tissue, with cell outlines indistinct, nuclei vesicular and ovoid or round. The stroma was very delicate and stained only faintly with eosin. There were masses of adult hyaline cartilage surrounded by an active perichondrium imbedded in the stroma. There were also many glandlike cystic dilatations lined by various types of epithelium, some columnar, some stratified squamous, some pseudostratified and others undifferentiated embryonal epithelial. However, there was no break in the basement membranes, and in any one gland the epithelium was regular and uniform. Some of the cysts contained coagulated fluid. There were also some collections of undifferentiated small round cells with hyperchromatic nuclei, which seemed to show occasional mitotic figures although it was difficult to make this out with certainty.

Microscopic Diagnosis.—Teratoma.

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MELANOMA OF THE FEMALE URETHRA

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MELANOMA is a highly malignant pigmented tumor, commonly described as arising from a pigmented nevus of the skin. Melanoma of the vulva, clitoris, rectum, adrenal and other parts of the body have been reported. Melanoma of the external orifice of the female urethra is a most unusual rarity, hence we feel a report of this case is indicated.

CASE REPORT

A white female, aged sixty-four years. Moderately obese with no complaints or symptoms except the pressure of a tumor near the urethra which troubled her when walking. Self inspection revealed a growth at the urethral opening.

Her family and past history were irrelevant. She had an uneventful menopause ten years ago. General physical examination revealed the patient to be in good condition for her age.

authors recommend the use of Siebold scissors to amputate the teratoma at its base and then remove the tumor by morcellation. Hirst recommends version or embryotomy.

The prognosis for the baby is usually hopeless; by far most are lost during delivery, the remainder die within a short time after delivery. The mother's prognosis is good.

M. L., a Porto Rican, thirty-eight years old, was admitted to Harlem Hospital Oct. 17, 1935. Menstruation normal, last period in January, 1935, due October, 1935. Obstetric history, gravida v, para iv. All previous deliveries were normal. The babies weighed between 7 and 8 pounds.

The patient registered in the out-patient department when she was six months pregnant, and her physical examination at this time was negative. Pelvic measurements were normal. The Wassermann was negative. When patient returned the following month, there were no abnormal findings. This was her last visit until admission to the hospital two months later.

On Oct. 17, 1935, in the morning, the membranes ruptured. She had no pains and remained at home doing her housework. At 6:30 P.M. of the same day she had one



Fig. 1.

sudden, severe pain and expelled the fetus up to the umbilicus where it became impacted. She claims the baby died after making two voluntary movements. A physician was called but his attempts at delivery were futile. One hour later the patient was admitted to the Harlem Hospital. She was in good condition; temperature 99°, pulse 96, respiration 20, and blood pressure 120/70. The uterus, which was soft, not tender, and freely movable, was at the level of the umbilicus. No fetal parts were felt, and no fetal heart was heard.

Vaginal examination revealed a partially delivered dead baby from vertex to umbilicus. Under ether anesthesia it was found that the cervix was fully dilated. At the level of the fetal sacrum a large partly cystic and partly solid mass which was obstructing the delivery could be felt. The cystic mass was perforated and about 4 ounces of clear yellow fluid was expressed. It was then possible to deliver both feet, traction downward resulting in the expulsion of a large loculated mass attached to the sacrum of the baby.

The placenta and membranes were expressed completely, causing but slight hemorrhage. The perineum was intact, and the patient left the table in good condition.

She left the hospital on her sixth day against our advice. Up to this time she had an uneventful postpartum course.

In June, 1935, the growth began to spread very rapidly and the patient went to bed where she remained until her death, June 25, 1935. At the time of her death the melanoma had covered the entire vulva and vagina. The inguinal lymph nodes on both sides were involved and broken down, discharging a very fetid, reddish fluid. The cause of death was septicemia from the marked involvement of the growth. There was no clinical evidence of metastasis to liver, lungs, brain, or other vital organs. Unfortunately an autopsy could not be obtained.

DISCUSSION

In searching the literature very carefully we are able to find only six other cases of melanoma of the female urethra reported, those by Reed,¹ Küstner,² Sängner,³ Koerner,⁴ Rosenthal,⁵ Auer.⁶ There is a difference of opinion as to the pathology of this malignant growth. Some authors contend that it is a melanosarcoma, others claim it is a melanocarcinoma. Graves,⁷ Braasch,⁸ Koerner,⁴ Tausig,⁹ Ewing¹⁰ and others agree that the sarcomatous or carcinomatous nature of the lesion is usually a very difficult decision to make. However, Broders¹¹ claims the proper classification is one of melano-epithelioma. Frequently the diagnosis is made with reservations. This is well understood when we consider how variable these lesions may appear histologically. Along with melanoblastomas of the vulva in general, these tumors contain a pigment varying in shades of black or blue. They tend to spread by lobes or knots or more extensively through superficial lymphatics. Sometimes, as in this case, the transportation of pigment can be demonstrated.

Frequently the local lesion tends to heal without delay after excision, only to have hopes banished by fatal metastasis elsewhere. Peculiarly true is the lack of local symptoms accompanying most of these lesions.

TREATMENT

The variable nature together with abundant properties of malignancy renders these tumors unalterable to x-rays, radiation or surgery with any degree of success. Nowhere does one find encouraging suggestions of therapy for the case at hand. Surgery is definitely limited because of the anatomical relationships which must not be disturbed for practical or esthetic reasons.

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In February, 1932, a mass thought to be an innocent caruncle was excised from the urethra. This reappeared in November, 1932, with a different morphology and was removed (Fig. 1). Grossly the tissue appeared brownish black in color, vascular, and spongy in consistency. The pathologic report read: "The pigment is yellowish brown and is found between the cells. Some of it, however, is being taken up by phagocytic cells. The stroma is fairly dense with a definite tendency for the arrangement of the cells in nests."

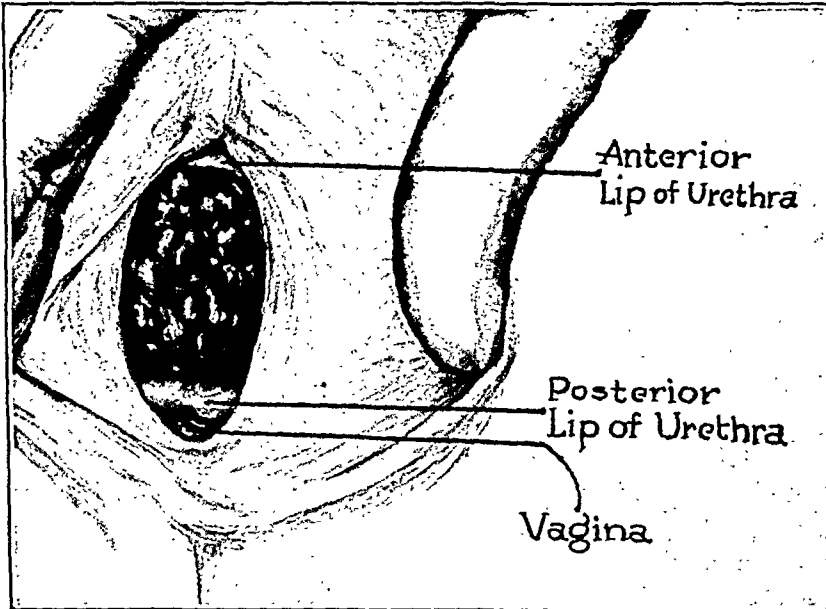


Fig. 1.—A drawing showing the growth of the urethra. The lips of the vulva are separated exposing the melanoma.



Fig. 2.—A low power photomicrograph of a section of the tumor. Note the large amount of pigment present.

Diagnosis.—Melanoma (Fig. 2). This growth was removed ten times and it always rapidly recurred, regardless of what form of treatment was given. It was cauterized with the actual cautery five times, using "cherry" heat. It was radiated four times with radium, by implanting 50 mg. of radium directly into the urethra for eight hours each time, and on one occasion deep x-ray therapy (200 K.V.) was given. The condition always showed improvement after radiation but within two to three months the growth would be as large and as ugly as before treatment.

Department of Maternal Welfare

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REVISION OF BIRTH, DEATH, AND STILLBIRTH CERTIFICATES

A BRIEF REPORT BY THE SUBCOMMITTEE ON CAUSES OF MATERNAL,
FETAL, AND NEONATAL DEATH OF THE AMERICAN
COMMITTEE ON MATERNAL WELFARE*

IN APRIL, 1937, the American Committee on Maternal Welfare appointed a subcommittee (1) to consider the causes of maternal, fetal, and neonatal mortality in relation to the forthcoming revision of the International List of Causes of Death, the rules of procedure for assigning cause, the revision of the birth and death certificates; and (2) to make suggestions directed toward securing information on a nationwide scale prerequisite for planning an effective program for the reduction of mortality from these causes.

The subcommittee calls attention to the magnitude of the loss of life from these causes and conditions, practically all of which are connected with pregnancy and childbirth. The total loss from these causes in the United States amounts to more than 150,000 lives each year. The total loss in 1935, as shown by the Bureau of the Census figures, was 161,249 lives, including 14,296 maternal deaths (12,544 deaths assigned to pregnancy and childbirth and 1,752 deaths in which pregnancy or childbirth was a complicating factor), 77,119 stillbirths, and 69,834 infant deaths in the first month of life, of which 56,262 were due to prenatal and natal conditions.

The total loss arising from these causes connected with pregnancy and childbirth is, however, far greater than is indicated by the information obtained from the registration of births and deaths. Many maternal deaths following early abortion probably go unregistered as such. The registration of stillbirths is generally recognized as incomplete. Many mothers who survive childbirth do so with impaired health.

With the continuing decline in the birth rate it becomes imperative to develop statistics prerequisite for planning an effective program for the reduction of mortality due to conditions of pregnancy and childbirth. The loss of life in the United States as shown by the maternal mortality rate is high and has not been markedly reduced during the period of record (1915-35). Our neonatal mortality and stillbirth rates also continue high and fail to show marked reduction. Before we can hope for effective reduction of these losses, accurate nationwide information, which will reveal the conditions underlying this mortality, must be made available. This information is within the possibility of collection through the regular channels of birth and death certification. The certificate forms and the statistical procedures must be revised to provide the prerequisite information.

*This report was accepted and approved by the American Committee on Maternal Welfare, Sept. 21, 1937.

GONOCOCCIC PERITONITIS IN PREPUBESCENT FEMALES

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CONTRARY to recorded opinion, gonococcic peritonitis in prepubescent females is not rare. I am able to report 16 cases which have occurred during the past two years. A thorough search of the literature reveals but 55 reported cases,¹ which together with mine make a total of 71. The reason for this report is to point out the frequency with which gonococcic peritonitis occurs in immature females, since in the past I have seen a number of cases diagnosed appendicitis or explored to rule out appendicitis.

Holt and McIntosh² point out that this disease is seen in children but not in infants. This is true for the reason that the cervix acts as a barrier. The cervix is seldom infected in children under 6, prepubescent development of its epithelium not yet having been attained. However, it can and does occur in young children since 2 of our 16 patients were four years of age. Our oldest was ten, and none had reached puberty. All were proved by positive smears and had the characteristic clinical finding in the lower genital tract, polypoid urethritis. Symptoms of peritonitis were usually present for forty-eight hours, and tenderness was localized deeply in both lower abdominal quadrants, rigidity was moderate and could be overcome by steady gentle pressure, and vomiting was absent. Average highest temperature and leucocyte count during the acute phase was 102.8° F. and 22,679, respectively. All subsided in a few days with cleansing intravaginal douches. After localization in the fountain-head focus, the cervix, electrocauterization was performed with excellent results.³ None suffered exploratory laparotomy.

CONCLUSIONS

1. Gonococcic peritonitis is occasionally seen in prepubescent females and should be borne in mind when considering differential diagnosis of acute abdominal conditions.

2. Treatment, during the acute phase, is supportive and exploration should be performed only after due consideration. Electrocauterization of the cervix, during the chronic phase, gives the best assurance of cure.

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1. *For Deaths in Which Pregnancy or Childbirth Occurred Within Three Months Prior to Death.*—(a) Was woman delivered or did death occur before delivery? (b) Period of gestation in terms of weeks? (c) If delivered, was child born alive or dead? (d) Week of gestation in which woman came under supervision of attendant at death? (e) Complications of pregnancy? (f) Complications of labor and delivery? (g) Postpartum complications? (h) Number of days between delivery and death of mother?

2. *For Deaths in the First Month of Life.*—(a) Weeks of gestation at birth? (b) Complications of pregnancy? (c) Complications of labor and delivery? (d) Physical defects in child at birth? (e) Postnatal conditions which contributed to death?

D. CAUSES OF MATERNAL DEATH DIRECTLY DUE TO PREGNANCY, LABOR, AND PUERPERIUM

The subcommittee has considered the causes of death as listed in the 1929 International List of Causes of Death and the Manual of Joint Causes (1933) as directly due to the puerperal state. It finds: (1) That certain types of causes fundamentally puerperal in nature fail to be included in Group XI, Diseases of Pregnancy, Childbirth and the Puerperal State; (2) that the cause classification for Group XI does not afford information showing the fundamental causes of maternal death; and (3) that many terms now accepted as indicating the cause of maternal death fail entirely, when mentioned alone, to give an accurate description of the cause of death. This section of the report covers these three aspects of mortality due to pregnancy, labor, and the puerperium.

1. *Types of Causes to be Included in Maternal Deaths.*—The subcommittee at this time limits its recommendations with respect to additional diseases and conditions to be considered as directly due to pregnancy, labor, and the puerperium to deaths of the following types: (a) Maternal deaths with mention of chronic nephritis (about 228 maternal deaths certified with mention of chronic nephritis were assigned to chronic nephritis in 1935). (b) Maternal deaths now assigned to violence and accidents, which include criminal abortions (259 deaths certified in these terms were assigned to violence and accidents in 1935).

2. *Cause Classification for Maternal Deaths Due to Diseases and Conditions of Pregnancy, Labor, and the Puerperium.*—The subcommittee points out that there are only four fundamental causes of maternal death—infection, toxemia, hemorrhage, and trauma. It recognizes that deaths prior to the 28th week of gestation (the period of previability) in general constitute a maternal and fetal problem separate and distinct from deaths that occur from the 28th week onward (the period of viability).

The general plan recommended for assigning cause of death under this classification¹ is that infection should invariably take precedence over every other puerperal disease or condition with which it was simultaneously mentioned. Hemorrhage should take general precedence over other puerperal diseases or conditions with the exception of infection. Toxemia should take general precedence over other puerperal diseases or conditions with the exception of infection or hemorrhage.

3. *Undesirable, Nonacceptable Terms for Certifying Cause of Maternal Death.*—The subcommittee presents a list of terms undesirable and nonacceptable for certifying cause of maternal death (Appendix I). The terms recommended to be considered

¹The full report of the subcommittee included a list of causes of maternal death recommended for consideration in connection with the 1938 revision of the International List of Causes of Death. The recommended list has been favorably considered by the Committee on Accuracy of Certified Causes of Death of the American Public Health Association and the U. S. Bureau of the Census.

A. REVISION OF THE STANDARD BIRTH CERTIFICATE

The subcommittee points out the great need for medical information with respect to all births (live and still). For the reduction of mortality connected with birth, accurate information must be made available with respect to prenatal and natal conditions. This information is prerequisite, not only for the reduction of fetal and infant deaths, but also for the reduction of maternal deaths and for the improvement of maternal and child health.

The subcommittee recommends that the standard birth certificate used for registration of both live and stillbirths be revised to include the following information:

1. Evidence of life at birth, i.e., breathing, movement of voluntary muscle, heart beat; or no evidence. (To be used for statistical purposes in classifying the birth as live or still.)

2. Period of gestation at delivery in terms of weeks.

3. Week of gestation in which mother first came under supervision of attendant at birth.

4. Complications of pregnancy.

5. Complications of labor, including statement as to whether delivery was natural or operative, and if operative the name of the operation.

6. Physical defects in the child at birth, especially defects which are or may result in crippling.

7. Time of fetal death with respect to labor. If the delivery was operative, the time of fetal death with respect to operation. (Applicable for stillbirths only.)

The subcommittee recommends that the definitions of stillbirth and live birth, as incorporated in the Rules of Statistical Practice of the American Public Health Association, appear on the reverse side of the standard birth certificate.

B. REVISION OF THE RULE WITH RESPECT TO MENTION OF CHILDBIRTH
ON DEATH CERTIFICATES

The subcommittee considers that the present instruction with respect to mention of childbirth on death certificates is inadequate to cover deaths associated with puerperal causes. The instruction as now stated in notes to the International List of Causes of Death, 1929 revision, page 15, and in the Physicians' Pocket Reference, 1931 edition, page 15, reads:

“Whenever parturition or miscarriage has occurred within 1 month before the death of the patient, the fact should be certified, even though the childbirth may not have contributed to the fatal issue.”

This instruction should be revised to read:

“Certification must be made for all deaths of females 15 to 49 years of age as to whether the patient was known to have been pregnant or to have been delivered of any product of conception within the 3 months prior to death.”

C. REVISION OF STANDARD DEATH CERTIFICATE

The subcommittee recommends that special items be incorporated in the standard death certificate applicable for all deaths in the first month of life and all deaths of women associated with pregnancy and childbirth. It recommends the inclusion of one question on the face of the certificate applicable for all deaths of females fifteen to forty-nine years of age:

“Was this female pregnant or delivered of any product of conception within the three months prior to her death?”

It recommends that questions adapted to obtaining the following information regarding conditions associated with pregnancy and childbirth be shown on the reverse side of the certificate:

No recommendations are presented at this time with respect to the precedence to be given in instances where two or more conditions are certified simultaneously. The subcommittee recognizes the importance of such recommendations and anticipates giving thorough review to methods of assignment procedure as soon as the necessary statistical information is made available for its use.

No recommendations are presented with respect to the classification of causes of stillbirth. The subcommittee is interested in securing the findings of the special study, Causes of Stillbirth, being made by the Children's Bureau with the cooperation of the Subcommittee on Stillbirths of the American Public Health Association which includes 6,750 schedules supplied by 229 hospitals located in 25 States and the District of Columbia, and also the findings from other special studies being made in several sections of the country.

No recommendations are presented at this time with respect to the classification of causes of infant death due to prenatal and natal conditions. The cooperation of the obstetric and pediatric societies will be sought.

The future work of this subcommittee will include consideration of (1) rules of procedure for assigning cause of maternal death; (2) classification of cause and rules of procedure for assigning cause of stillbirth; (3) classification of cause and rules of procedure for assigning cause of infant death due to prenatal and natal conditions which occur mainly in the first month of life.

ROBERT L. DENORMANDIE, M.D., *Chairman*

GEORGE W. KOSMAK, M.D.

PHILIP F. WILLIAMS, M.D.

ELIZABETH C. TANDY, Sc.D.

APPENDIX I

List of Undesirable, Nonacceptable Terms for Certifying Cause of Maternal Death

Abnormal labor	Displacement of pregnant uterus
Abnormal parturition	Dropsy of amnion
Abortion	Dystocia
Accident of labor	Embryotomy
Accident of pregnancy	Evacuation of uterus
Accidental abortion	Faulty presentation (mother)
Accouchement	Fissure of nipple, puerperium
Application of forceps	Fistula of breast, puerperal or un-
Atony of uterus during parturition	qualified
Breech presentation	Following childbirth
Cephalotomy	Foot presentation
Cephalotripsy	Forced delivery
Cesarean operation	Forceps operation
Childbed	Galactocoele
Childbirth	Galactorrhoea
Confinement	Gestation
Consequence of labor (mother)	Hebotomy
Craniotomy	Hydramnios (mother)
Criminal abortion (mother)	Hydrops amnii
Cyesis	Hydorrhoea gravidarum
Dead fetus in uterus	Hydorrhoea in pregnancy
Deformed pelvis (female 15-44 years)	Hysteralgia of pregnant uterus
Delayed delivery	Immature birth
Difficult labor	Immaturity
Disease of placenta	Induced abortion

as undesirable and nonacceptable for certification are those which fail entirely, when mentioned alone, to give definite information with respect to the cause of maternal death. The subcommittee recommends that this list of undesirable terms be added to those set forth in the 1929 revision of the International List of Causes of Death, and that whenever a death is certified as due to any of these undesirable terms the local registrar should require an explicit statement from the reporting physician as to the cause of death, the explicit statement to be expressed in so far as possible in terms which are "approved" or recommended for use.

In making this recommendation the subcommittee is cognizant of the work entailed upon both registration officials and physicians in connection with obtaining satisfactory information regarding cause of death. It points out that accurate statistics with respect to the cause of maternal death are the first prerequisite for planning an effective program for the reduction of maternal losses. It believes that the usefulness of the statistics may be greatly enlarged through the cordial cooperation of the medical profession and the registration officials.

E. SUPPLEMENTARY TABULATIONS BY THE BUREAU OF THE CENSUS

1. *Deaths Associated With Pregnancy and Childbirth.*—The subcommittee calls attention to the great need for information on maternal deaths associated with pregnancy and childbirth and to the fact that no published statistics are available for the United States later than for the year 1925. Several foreign countries have published such statistics much more recently than the United States; the majority of these countries published the statistics annually.

It is recommended that the United States Bureau of the Census tabulate and publish annually statistics showing the total number of deaths in which pregnancy and childbirth are mentioned on the death certificate, by primary and principal contributory cause of death, and the puerperal condition mentioned on the certificate for deaths in which the puerperal state is mentioned but is not considered either a primary or a principal contributory cause.

2. *Deaths in the First Month of Life.*—The subcommittee calls attention to the fact that there are unquestionably many more deaths in the first month of life due to prenatal and natal conditions than can be classified as such from the statistics made available in "Birth, Stillbirth, and Infant Mortality Statistics," where the short list of causes is used. The figures in "Mortality Statistics," where the detailed International List of causes is used, show that many deaths grouped together under "All Other Causes" in the short list are essentially due to prenatal and natal causes which are operative in the first month, notably diseases of the thymus, hemorrhagic conditions, and cerebral hemorrhage.

The subcommittee recommends that the United States Bureau of the Census issue an annual tabulation of deaths under 1 month, showing detailed information for each cause title of the International List similar to that now shown in "Mortality Statistics" for deaths under 1 year and for deaths at older ages. This recommendation is not to be interpreted as suggesting that the subcommittee is not cognizant of the objections to the present list and not desirous of securing at the earliest possible date a revision of the list of causes of death applicable to the first month of life. This information on cause, as tabulated under the 1929 revision of the International List, is needed for the work on the revision of causes of neonatal death.

F. WORK IN PROGRESS

The conclusions and recommendations offered by the subcommittee at this time cover only a few of the major aspects of the work with which it is charged.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology

The seventh volume of *Handbuch der speziellen pathologischen Anatomie und Histologie*²¹ deals with diseases of the ovaries, written by John Miller of Wuppertal-Barmen. The previous installments, VII/1, dealt with the uterus and tubes, and VII/2 with the pelvic connective tissues and uterine ligaments. This concludes the female genital organs. The volume is of large size, 1,047 pages.

There are 5 main divisions, a short normal anatomy and physiology; the diseases of the ovary including inflammatory troubles and granulomatous involvements, and simple nonneoplastic cysts; neoplasms; parasites and foreign bodies; injuries of the ovary.

The anatomic description is very summary. Decidual reaction is considered entirely normal in pregnancy and independent of inflammatory irritation. The physiology although short, is up to date and informative. Malformation and deviations in form, size, and position are taken up. An excellent discussion of ovarian pregnancy is given. More space is devoted to tuberculosis of the ovary than to the other inflammatory infections.

A good classification of simple nonneoplastic cysts is offered. These are not considered retention cysts. Among them are included the lutein cystic formations. Endometriosis of the ovary with all the theories offered is well described.

A new classification of neoplasms is offered. There are 2 main divisions, (1) the ripe homeotypic, clinically benign, forms and (2) the unripe, heterotypic malignant forms. Each of these is subdivided into connective tissue, epithelial and teratoid growths. Endothelioma of the ovary is called a mere fiction. Pseudomucinous cystomas are classified under teratoid growths as first proposed by Bland Sutton in 1888.

Under Classification 1, namely homologous or homeotypic, neoplasms of epithelial derivation, the author places serous surface or ciliated tumors such as fibroadenoma and cystomas of the ovary, a classification which does not clarify the situation.

Particular emphasis is placed upon the newer subgroupings which are attracting much discussion in the literature at the moment. Of these, an excellent presentation of Brenner tumors, oophoromas, is given. Although Schiller's classification of basal cell carcinoma is fully concurred in by the author, he has not as yet separated this grouping; basocellular epitheliomas with granulosa cell tumors and basal cell carcinomas, clinically malignant, are still grouped together. The estrogenic potency and consequent physiologic effect upon the uterus of the granulosa cell tumors is well brought out. A detailed description of both seminoma and arrhenoblastoma are

²¹Handbuch der speziellen pathologischen Anatomie und Histologie. Siebenter Band; Dritter Teil: Die Krankheiten des Eierstockes. John Miller. Mit 145, zum Teile farbigen, Abbildungen. 1017 Seiten. Verlag von Julius Springer, Berlin, 1937.

Induced premature labor	Prolapse of pregnant uterus
Inertia of uterus	Prolonged labor
Instrumental delivery	Protracted labor
Intentional abortion	Puerperal accident
Labor (unqualified)	Puerperal apoplexy
Laparoelytotomy	Puerperal disease of breast -
Malpresentation	Puerperal fissure of nipple
Mammary fistula	Puerperal fistula of breast
Menstruation during pregnancy	Puerperal displacement of uterus
Miscarriage	Puerperal fistula of mammary gland
Missed abortion	Puerperal galactophoritis
Missed labor	Puerperal state
Multiple birth	Puerperium
Multiple parturition	Result of labor (without further ex-
Multiple pregnancy	planation)
Neuralgia of pregnant uterus	Retarded labor
Obstetric operation	Retention of dead ovum
Overdistention of uterus	Retroversion of pregnant uterus
Parturition	Spontaneous abortion
Perineorrhaphy	Spurious labor pains
Porro operation	Subinvolution of uterus
Pregnancy	Symphiseotomy
Pregnancy in abnormally formed uterus	Transverse presentation
Premature birth	Version during labor
Premature delivery	

Cotte, G.: What Place Have Autogenous Ovarian Grafts in Gynecologic Therapy, *Gynécologie* 35: 641, 1936.

Cotte is firmly convinced of the value of autogenous ovarian grafts. The two chief indications for this procedure are sterility and prevention of menopausal symptoms. To overcome sterility, an ovary may be transplanted into the uterine cavity or in the uterine cornua. Ovarian grafts may also be used to conserve menstruation or to prevent disturbances of the climacteric following castration. The author is of the opinion that a castrated woman is not a normal individual. He also believes that in spite of the recent advances in endocrinology, we cannot prevent or overcome the disturbances which follow castration. Hence in such cases ovarian grafts have their most important indications.

In cases of salpingitis Cotte prefers to leave the uterus, because he believes that persistence of menstruation is the best guaranty for continued function of the ovaries. Leaving the uterus, therefore, is a far better procedure than performing subtotal hysterectomy and grafting an ovary under the skin.

J. P. GREENHILL.

Zappi, F., and Costanzo, E.: Severe Hemorrhage Due to Rupture of the Hymen Following Coitus, *Clin. obstet.* 15: 9, 1937.

The author reports the case of a very severe hemorrhage following defloration of the hymen and briefly comments on the mechanism, the diagnosis, and the cure of such an infrequent lesion.

AUGUST F. DARO.

In the course of the many operations performed for sterilization, for feeble-mindedness and inheritable diseases, von Mikulicz-Radecki has had ample opportunity to observe the normal pelvic organs at various stages of the menstrual cycle. He found that about twelve days after the beginning of the menstrual cycle profound changes occurred in the relationship between the tube and ovary in that the tube, the fimbriated extremity and the mesosalpinx formed a barrier around the ovary. This cyclical anatomic finding he terms the "bursa-ovarica stellung," and finds that it almost completely shuts off the ovary from the peritoneal cavity. This predisposes to a rupture of the matured follicle into the lumen of the tube. This phenomena is discussed at length in its relation to the possible operative maneuvers suggested in the treatment of sterility. Where the tube cannot be freed to again perform this function he prefers cornual implantation of the ovary, with vascular pedicle, as originated by Estes.

—Philip F. Williams.

Vital statistics reveal as one of our social phenomena a continuous decline of the birth rate. As the author of *Childless: A Study of Its Causes and Treatment*²⁴ says: "From the first birth records (Sweden, 1750) to the present, each succeeding census in every part of the civilized world has shown a diminishing birth rate." As the curve downward became steeper a widespread interest has sprung up in the factors responsible for the falling birth rate. The modern study of sterility and its treatment really dates from the pioneer work of Hühner and Rubin and has been influenced by the stimulus of a coincident development in reproductive physiology.

To inform the public of the present status of our knowledge of sterility, Dr. Berkow presents this book. In the philosophic consideration of the underlying and historic phases of this problem, the author discusses the ancient beliefs and religious and legal aspects connected with sterility. He feels that contraception, which is the principal agent of the falling birth rate, plays a minor rôle in the production of childless marriages. The various theories, biologic predestination, the influence of civilization and other factors are assessed. The present nationalistic attitudes toward the problem are mentioned. The falling birth rate, the author says, is regarded as a national problem but the rising tide of sterility is still considered an individual one.

In the biologic aspects of reproduction he notes accurately the facts of conception and development and points them out. A discussion of the physiology of reproduction includes such topics as rhythm theory, development of abnormal body forms and the relationship of glandular influences and abnormalities of fertility. The chapter on the relationship of diet to fertility affords an opportunity for an explanation of the properties of the vitamins. The influence of congenital obstacles and gonococcal infections are clearly explained. There is a rational discussion of modern obstetrics in the chapter of one child sterility.

In the third part of the book the author rather briefly discusses the treatment of sterility. Fortunately he emphasizes the need and necessity for a prolonged study of both partners in a childless marriage. Again reverting to a philosophic attitude he answers with effectiveness how modern life can be reconciled with the question of sterility, and outlines the position of the state.

The pleasant manner in which the book is written and the easy style in which the medical problems are discussed make the book readily understandable by the general public.

—Philip F. Williams.

²⁴*Childless: A Study of Sterility, Its Causes and Treatment.* By Sam Gordon Berkow, M.D. Illustrated. 307 pages. Published by Lee Furman, Inc. 351 Fourth Ave., New York City, 1937.

offered. In all these new varieties of tumors dealt with, the illustrations are excellent and numerous; in contradistinction with this, the majority of the commoner forms of ovarian growths might well have received more illustrations.

It is impossible to give even an idea of the immense amount of material, well arranged, with comparatively easy reference to the literature contained in this volume. Both the clinical and pathologic aspects have been fully and adequately treated. The statistics of most of the types that have been fully accepted are mainly from the older literature, while the statistics dealing with the newer classifications are more recent. The reason for this is easily understandable. Both an authors and subject index conclude the volume. This publication will prove indispensable as a reference book for any one who desires to find the latest information and literature dealing with ovarian diseases.

—R. T. Frank.

This pamphlet, *Périodes de Fécondité et de Stérilité Chez la Femme*,²² forms one of a series on research and application in medicine and surgery published by Masson. Here Vignes and Robey discuss whether there exists absolutely a period of fertility and a period of physiologic sterility according to the findings of Ogino and Knaus. This new method of contraception is formulated on three statements: the expelled ovum has a very limited life, the spermatozoa have a very limited life in the genital passage of a woman, the ovum is produced at a fixed date in the menstrual cycle. In a succeeding chapter they discuss the life of the ovum, the travels and survival of the spermatozoa.

The unusual length of time in which spermatozoa can be preserved in vitro is compared with their short life in the genital tract of the woman. In discussing the artificial preservation of spermatozoa they mention such factors as the rôle of pH, of the osmotic tension, and of the temperature, and contrast this with what is known of such findings in the female. They do not believe that the spermatozoa survive for a greater period of time than forty-eight hours, although they admit that it is possible that the duration of such life may be variable. They question whether spermatozoa, which appear to be alive on their recovery from the genital passage after a period of twenty-four hours, might be capable of fertilization. In the third chapter they discuss the known factors of ovulation and recount the exceptions which have been noted. The particulars of practical application of the method of Ogino-Knaus are given and are followed by various pertinent criticisms.

While the authors believe that the time of ovulation is a fixed point in the menstrual cycle of the woman, they conclude, however, that there are valid objections, and that there appear to be no criteria which permit one to say that a woman is either going to be normal or exceptional. An excellent bibliography on the subject is appended.

—Philip F. Williams.

Von Mikulicz-Radecki in a contribution read before the Koenigsberg Scientific Society, *Der Eiauffangmechanismus bei der Frau und seine Bedeutung für die Sterilität*,²³ discusses the probability of a protective mechanism whereby the ovum expelled from the ruptured follicle reaches the lumen of the tube. The various theories advanced to explain this migration are weighed. The physiology and anatomic relations at the time of ovulation in various animals are described.

²²*Périodes de Fécondité et de Stérilité Chez la Femme*. Par H. Vignes et M. Robey. 85 pages. Masson et Cie, Paris, 1936.

²³*Der Eiauffangmechanismus bei der Frau und seine Bedeutung für die Sterilität*. Von Felix v. Mikulicz-Radecki, Max Niemeyer, Halle (Saale), 1937.

There are short concise introductory chapters on the history of endocrinology, embryology, etc. One hundred and eighty pages are devoted to a description of the various glands of internal secretion. These all are ample, clear, and up-to-date, based on careful utilization of the literature. The chapter on the physiology of estrone is particularly good. An excellent chapter on the chemistry of the sex hormones follows. As is to be expected in a developing branch of medicine, many of the subjects dealt with, permit of various interpretations. However, when the author speaks of a brain sex center and of a bleeding hormone, it should have been emphasized that these two concepts are largely hypothetical and illustrate personal views. Kurzrok accepts as definitely proved that the follicle-stimulating and luteinizing hormone of the anterior pituitary are separate entities.

A large portion of the book is devoted to the application of endocrinologic knowledge to the treatment of gynecologic and obstetric disturbances. It may be stated that the author is a very active and optimistic therapist. On the other hand his description of the syndromes is clear, understandable and accurate. The text is illustrated by excellent figures and by accurate case histories which show a thorough workup of the patients. To a reader familiar with the personal factors which still must so largely enter into the interpretation of diagnosis and therapy in endocrinology, this book should prove of utmost value. The general practitioner may find the methods advocated less effective than anticipated, when applied. Each chapter has a valuable bibliography which will prove of equal use to both the laboratory worker and the clinician. The book contains an immense amount of information otherwise to be obtained only by intensive and laborious delving into the literature, which has attained colossal proportions.

—R. T. Frank.

Fels' *Hormone of the Corpus Luteum*²⁹ is a monograph covering the biology, chemistry, and therapeutic application of this hormone. Fels has been a pioneer in this field and together with Slotta was one of the first to isolate and obtain this hormone in crystalline form. Much of his work was done in Breslau at the Klinik Fraenkel, and continued and completed at the Lying-In Institute of Buenos Aires. Consequently it is written from a personal standpoint and based upon personal investigation. Of the tests, he prefers the Corner to the Clauberg or Knaus test, although the Clauberg reaction is more delicate than the Corner method.

In these pages an excellent presentation of our knowledge of the subject will be found, with a very satisfactory exposition of the entire subject, including the literature.

The subjects covered are historical, introductory, the tests with their modifications, methods of standardizing the hormone, especially the biologic effects produced. Fels is convinced that the separation of the symphysis noted in the guinea pig is due to the estrogenic hormone. He likewise gives a full description of how the yellow body reacts on the hypophysis, the breasts, and nidation. The biologic relation between the estrogenic and corpus luteum hormone is discussed. That this hormone like the others is not species specific has been amply proved. It can be found only in the yellow body and the placenta, and has been demonstrated in the blood and urine although in very small concentration. The effect of the corpus luteum hormone on the male genital tract is also taken up. The excellent chapter on chemistry and synthesis of the hormone was written by Slotta (now in São Paulo, Brazil). The concluding chapter deals with the therapeutic application of progestin. This monograph is a valuable contribution.

—R. T. Frank.

²⁹Das Hormon des Corpus Luteum. Von Dr. Erich Fels, Instituto de Maternidad de la Sociedad de Beneficencia, Buenos Aires. Mit 40 abbildungen im text, 169 seiten. Franz Deuticke, Wien, 1937.

*Carcinoma of the Female Genital Organs*²⁵ by Malinowsky and Quater was translated from the Russian by A. S. Schwartzmann. It is a monograph of 11 chapters written by 10 different Russian physicians. Just why this monograph was selected for translation is not apparent to me as it contains nothing either startlingly new in its observations or presentation.

As might be expected, when such a subject as the etiology of carcinoma is dealt with, this chapter boils down to the possible causes as chronic irritation and embryonal cells. Calcium intravenously is suggested for inoperable carcinoma. The concluding chapter deals with the disability produced by carcinoma of the female sex organs.

—R. T. Frank.

Crossen and Crossen's *Synopsis of Gynecology*,²⁶ second edition, is far superior to the usual run of synopses. A great deal of information is concisely and understandably presented. Both the physiology as well as the examination of the patient are of unusual excellence.

Exception may be taken to a number of the statements. For example, on page 80, "hypoactivity of the gonad causes a masculine shift in the female and a feminine shift in the male." On page 114 "pelvic massage and dilatation of the cervix, under antiseptic precautions, aid in promoting ovulation." In comparison with other chapters, that dealing with relaxation of the pelvic outlet is quite insufficient. In the discussion of dyspareunia, the important psychic factor is entirely omitted.

—R. T. Frank.

The second edition of Benthin's *Therapy of Women's Diseases*²⁷ appears four years after the first one. The chapter on endocrine disturbances has been rewritten and enlarged. The book is designed mainly for the general practitioner.

It is noticeable that the modes of therapy advised in many instances differ greatly from those practiced in this country. For puberty bleeding, in addition to hygienic measures, curettage is advised early. In very stubborn cases, and as rarely as possible, x-ray can be used. Among the treatments for amenorrhea, hot sitz baths, uterine diathermia, estrogenic hormones, and to my surprise, curettage are advocated. In stubborn cases, so-called "irritative dosage" of x-ray to the ovaries is suggested. In the treatment of sterility, mention is made of Fruktulet, small perforated aluminum cervical drains, to be worn for several days after which intra-uterine treatment can be given, to minimize the resultant discharge. The book concludes with a formulary and additional hints for office practice.

—R. T. Frank.

Endocrinology

*The Endocrines in Obstetrics and Gynecology*²⁸ by Kurzrok has been written by an experienced laboratory research worker who has contributed substantially to research and who likewise has a large clinical experience. It is therefore a work of importance.

²⁵*Carcinoma of the Female Genital Organs*. By M. C. Malinowsky and E. Quater. Translated from the Russian by A. S. Schwartzmann, M.D. Illustrated, 255 pages. Published by Bruce Humphries, Inc., 306 Stuart Street, Boston, Mass.

²⁶*Synopsis of Gynecology*. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc. and Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Second edition. With 106 illustrations, 247 pages. The C. V. Mosby Company, St. Louis, 1937.

²⁷*Therapie der Frauenkrankheiten*. Von Professor Dr. W. Benthin. Koenigsberg i.P. Zweite, neubearbeitete Auflage. Mit 23 Abbildungen im Text, 210 Seiten. Urban & Schwarzenberg, Berlin und Wien, 1937.

²⁸*The Endocrines in Obstetrics and Gynecology*. By Raphael Kurzrok, Ph.D., M.D., Associate in Obstetrics and Gynecology, College of Physicians and Surgeons, Columbia University. Illustrated, 488 pages. Williams and Wilkins Company, Baltimore, 1937.

This *Synopsis of Genitourinary Diseases*²⁸ which appeared first three years ago now comes out in a second edition. It is felt that the recent advances in the treatment of genitourinary diseases have been of sufficient importance to warrant a second publication. Among the changes that appear in this edition is a very complete discussion of the regulation of the diet which has lately assumed an important rôle in the treatment of infections, and is regarded as important in the control of calculus formation.

In the discussion of nontuberculous infections of the genitourinary tract, there have been outlined a number of diets including a high vitamin acid-ash diet, various modifications of the ketogenic diet, with a low caloric value, and sample menus and lists of food values.

In the section on cryptorchidism the use of gonadotropic hormones is discussed as to its value and method of administration. The largest dose mentioned is 300 rat units, three times a week. The discussion of urogenic and functional disturbances of the bladder has been elaborated. The re-written section on disturbances of the male genital functions, especially in regard to sterility, should be of interest to those investigating nonfertile married couples.

—Philip F. Williams.

This book, *Kidney Pain, Its Causation and Treatment*,²⁹ brings before the medical public the views of the author on the subject of obscure kidney pain. The ideas expressed represent the results of an experimental attack on the problem made during the past decade, and, in addition, an attempt to explain obscure pain from a clinical standpoint. Particularly in the investigations the author has tried to evaluate the relationship of the kidney-pelvis musculature to obscure kidney pain.

After a chapter on embryology and anatomy of the kidney, the author describes the technic of pyeloscopy and pyelometry, through which he is able to determine the tone of the kidney-pelvis musculature. He feels that more than one type of dysfunction of the kidney structure may co-exist in the same patient, and outlines an investigation which may rule out various factors, local and general. A similar handling of ureteral dysfunctions is given.

The study of the pharmacologic and pharmacodynamic action of drugs on the urologic system has been carried out experimentally on the anesthetized dog, and clinically by urologic investigation of patients. During this investigation the method of pyeloscopy and pyelometry has been utilized. It is stated that there are experimental and clinical inconsistencies in the action of adrenalin and estrine, if one postulates that the actions of autonomic and sympathetic are antagonistic. Recitals of clinical cases are appended. After discussing hydropelvis and hydro-nephrosis, the author outlines the indications and suggestions for treatment in such conditions.

It is felt that the value of pyeloscopy and pyelometry have not been sufficiently emphasized in previous studies of kidney pain and other complications. The technic is so easy that it should be added to both clinical and experimental research on this problem, the solution of which, it is felt, will be more rapidly advanced by a closer liaison between the physiologist and urologist.

—Philip F. Williams.

²⁸*Synopsis of Genitourinary Diseases*. By Austin I. Dodson, M.D., F.A.C.S., Richmond, Virginia. Professor of Genitourinary Surgery, Medical College of Virginia; etc. With 112 illustrations. 294 pages. Second Edition. The C. V. Mosby Company, St. Louis, 1937.

²⁹*Kidney Pain, Its Causation and Treatment*. By J. Leon Jona, M.D., F.R.A.C.S., Hon. Asst. Gynaecological Surgeon, Women's Hospital in Melbourne. Illustrated. 94 pages. J. & A. Churchill, Ltd., London, 1937.

Kehrer has written a 564 page monograph on *Endocrinology and the Gynecologist*.³⁰ The title, however, might have been "The Causes of Amenorrhea." The author accepts prepuberal and postclimacteric amenorrhea, conditions of amenorrhea during which the ovarian function persists. He considers the cerebrum, the diencephalon, the uterus, and ovaries a biologic unit. A full and up-to-date analysis of the sites at which the various sex hormones originate and the tests for their demonstration is given. He accepts Seitz's classification of amenorrheas. An unusual casuistic, largely obtained from the literature, on anomalies, hermaphroditism, as well as on ovarian tumors some of which do and others which do not produce amenorrhea, is offered. Then come the endocrine syndromes in which amenorrhea is noted, including Froehlich's, Laurence-Moon-Biedl syndrome, lipodystrophy, acromegaly, brain tumors, etc.

An immense amount of material will be found in the pages of this monograph which is merely a source book covering a great deal of the literature. The value of this book is somewhat impaired by the incomplete bibliography, incomplete as to authors as well as to the sources of the references.

—R. T. Frank.

*The Rabbit Test*³¹ by Anklesaria is a monograph dealing with this test for pregnancy. The first 30 pages are introductory and give an extensive review of the literature dealing with the physiology of the female sex organs, as well as the diagnosis of pregnancy by other methods. The remainder of the monograph describes the technics, the application of the test, and a considerable casuistic material in which the test proved of value. Special emphasis is laid in distinguishing between normal and abnormal gestational conditions.

—R. T. Frank.

Miscellaneous

The third volume of *Post-Graduate Surgery*,³² edited by Rodney Maingot, has appeared. This volume which totals 2,000 pages, has many contributors, all English. As differences exist between English and American surgery, these contributions are of particular value, especially in debatable fields in which technics and indications have not yet crystallized.

The section devoted to obstetric surgery, by Bourne, is divided into 6 chapters. He emphasizes *what* to do over *how* to do it. His indications are very careful and given in detail. For induction of labor he favors rupture of the membranes or bags, believing, as I consider justly, that endocrine methods have not yet proved their value. He then takes up version, forceps, among which the illustrations show some patients in the lateral posture, as well as destructive operations. He is against the low cesarean operation in infections and states that the Latzko technic is difficult.

—R. T. Frank.

³⁰Endokrinologie für den Frauenarzt. Von Professor Dr. Erwin Kehrer, Geh. Med. Rat, Direktor der Universitäts-Frauenklinik in Marburg. Mit 34 abbildungen, 564 Seiten. Ferdinand Enke, Stuttgart, 1937.

³¹The Rabbit Test. By S. B. Anklesaria, M.D., Honorary Obstetrician and Gynecologist, Shet Vadilal Sarabhai General Hospital, etc., Ahmedabad. With a foreword by Dr. Emil Novak. 161 pages. H. K. Lewis & Co. Ltd., London, 1937.

³²Post-Graduate Surgery. Edited by Rodney Maingot, F.R.S. (Eng.). Volume III. With 1015 Figures in the Text. 2,000 pages. D. Appleton-Century Co., Inc., New York, 1937.

The chapter on anesthesia, the evaluation of surgical risks in different conditions, and every form of treatment utilizable in preparing a patient for and subsequent to operation, are very well handled. The author employs great care in giving the physiologic facts upon which different types of therapy are based. For example, his preliminary remarks introducing acidosis and alkalosis, show that he is aware that many medical men do not understand the underlying principles upon which the recognition and treatment of these disturbances are based.

Naturally in a book of this kind some improvements can be introduced. The chapter on shock is extremely short considering its importance. Whether every surgeon will agree that in heart and kidney diseases local anesthesia, supplemented by gas oxygen is to be preferred, is open to question. Likewise that in a diabetic, gas ether supplemented with ether or spinal anesthesia should be employed, is open to discussion. I note that only the most cursory mention of the sedimentation test, which certainly gynecologists find of tremendous help, is made. The bibliography appended at the end of each chapter should prove extremely useful. This is a good book.

—R. T. Frank.

During the World War, Dr. Guedel was concerned in the instruction and the supervision of the administration of anesthesia by untrained medical corps men. His observations in those days and his continuing interest in the subject in intervening years has resulted in a technic of teaching anesthesia which he presents in this new book, *Inhalation Anesthesia*.⁴² The book is to be regarded as a fundamental guide, since the physiologic or pharmacologic mechanisms involved are discussed only in the line of clinical application.

The book is divided into two parts: Principles of Inhalation Anesthesia and Anesthesia Accidents. In the first part he discusses inhalation anesthesia by methods and agents, and continues with a discussion of the stages and signs, which he illustrates by means of graphic charts. The extent or depth of anesthesia required for the control of surgical reflexes is considered by systems and operation.

Surgery of the vagina is recommended to be performed under his suggested lower first plane. Normal delivery and low forceps extraction are also placed in this group. Deep anesthesia is not regarded as necessary to provide muscular relaxation in cesarean section. The major consideration here is the prevention of vomiting during the operation. The operation of internal podalic version and extraction is regarded as calling for anesthesia in the third plane. Bandl's contraction ring is considered to be amenable to the upper third plane. In the section discussing breech extraction the upper third plane anesthesia is considered until the breech is broken and one foot brought down, and the anesthesia then brought back to the upper second plane for extraction.

In discussing resuscitation of the infant, the author feels that this is facilitated if the maternal CO₂ level is high at the time of delivery. This may be utilized safely with head presentations, but the after-coming head calls for a low maternal CO₂ level for two or three minutes prior to delivery, or else premature inspiration, with resultant aspiration of fluid or débris, will occur. Hence with the CO₂ level low the first inspiration in breech extraction babies will be delayed as a rule. There is ample discussion of the preparation of the patient and selection of the anesthetic agent.

The second half of the book is devoted to a consideration of anesthetic accidents, difficulties and deaths under anesthesia. In this section the author discusses the various factors of blood pressure, ventricular fibrillation, central respiratory failure,

⁴²*Inhalation Anesthesia*. By Arthur E. Guedel, M.D., Associate Clinical Professor of Surgery (Anesthesia), University of Southern California School of Medicine. 172 pages. The Macmillan Co., New York, 1937.

The second edition of Warbasse's *Surgical Treatment*,⁴⁰ now Warbasse and Smyth, appears eighteen years after the first one. It is a one man job in 3 volumes of together 2,600 pages. As can be seen from the title, treatment is its sole purpose, both diagnosis and pathology being omitted. Presumably it is therefore meant for the practicing surgeon and as an adjunct for those medical men who participate in the choice of operation and aftertreatment. The entire field of surgery is covered.

Volume I deals mainly with the general principles of surgery, including anesthesia. Under anesthesia, local anesthesia for special operations is given in great detail. On the other hand, nutritive disturbances and endocrinopathies are summarily dealt with in 2 pages. There is a long and detailed chapter on the blood and blood vessels, with a well-illustrated portion dealing with the anatomy and the ligation of various major vascular trunks. Over 300 pages are devoted to the diseases of bones, fractures, dislocations, joints, and operations on these structures. Then muscles and tendons are discussed. A chapter dealing with the skin and appendages would appear to me more appropriate in a book on dermatology. A long roster of dermatologic lesions is given, with their treatment, which to the average surgeon or practitioner can be of little value unless he has received exceptional dermatologic training.

In Volume II the head, including the brain, the eye, ear, mouth, and nose, as well as larynx and trachea will be found. The spine, neck, thorax, breast, abdomen, stomach, spleen, and pancreas are likewise discussed in this volume.

The third volume covers hernia, rectum, vermiform appendix, liver and gall-bladder; also the genitourinary organs, extremities, pelvis, amputation. Special chapters are devoted to plastic and cosmetic surgery. Surgery of the newborn, electricity and radium, first aid and bandaging, are discussed and concluding some chapters on economics. The index forms a special small volume of 131 pages.

This surgery covers an immense amount of territory in a very uneven fashion. Some subjects are dealt with in detail, as for example local anesthesia of the various regions, the ligation of larger vessels, tonsillectomy, appendectomy, etc. Other subjects are dealt with so cursorily as to prove of little value. The description of the major operations in most instances is far too sketchy to be utilized by any but the fully trained surgeon. I mention for instance, laryngeotomy in one stage and transplantation of ureters into the sigmoid. Exceptions, in which a detailed description is given, are thyroid resection, amputation of the breast, the general principles of entering the abdomen and treating intraabdominal conditions. In these subjects the text is adequate and fully illustrated. In the operation for inguinal hernia, reliance is placed on the transversalis and the external oblique aponeurosis without transplantation of the cord. In femoral hernia the closure of the ring below Poupart's is stressed. The operation for cystocele does not conform to the most modern technic.

—R. T. Frank.

*Preoperative and Postoperative Treatment*⁴¹ is a very detailed account of the most modern methods, particularly those practiced by the younger group in Boston. A number of others have aided the author in writing special chapters.

The book contains a tremendous amount of material, well arranged and readily accessible. The most modern methods of diagnosis and preoperative care are described in great detail for every type of surgical affection.

⁴⁰*Surgical Treatment*. By James Peter Warbasse, Special Lecturer in the Long Island Medical College, etc., and Calvin Mason Smyth, Jr., Assistant Professor of Surgery in the University of Pennsylvania Graduate School of Medicine, etc. Second edition, in three volumes, with 2486 illustrations, some in colors; 2617 pages. With added complete index. W. B. Saunders Co., Philadelphia, 1937.

⁴¹*Preoperative and Postoperative Treatment*. By Robert L. Mason, M.D., Assistant in Surgery of the Massachusetts General Hospital. Illustrated, 495 pages. W. B. Saunders Company, Philadelphia, 1937.

and 172. In the closing chapters of the book are found discussions on complications, special procedures and surgical diets. The book closes with a list of medicolegal points. This is an excellent book for the surgical nurse or surgical resident.

—Philip F. Williams.

In this manual, *Operating Room Procedures*,⁴⁶ bound in an utilitarian loose-leaf fashion, Miss Hoppe and Miss Halverson have produced a guide for all who are concerned with the handling of operating room routines. This book should be of utmost advantage not only to the operating room supervisor, but to the surgical internes and staff as well. Included in the table of contents are sections on a general outline of the routines for the personnel, care and preparation of materials, draping, and various special trays and instrument set-ups. In the remainder of the book surgery is divided by systems, under each system pertinent operative procedures are given. Each procedure is discussed from the operating nurse's standpoint with a brief statement of the purpose of the operation, position and draping for the operation, technic, sutures and instruments used.

The book offers an excellent example of the manner in which the organization of a particular division of a hospital may be accomplished. The type of binding used will render changes and revision an easy matter.

—Philip F. Williams.

*Some Fundamental Aspects of the Cancer Problem*⁴⁷ is published by the American Association for the Advancement of Science and edited by Henry Baldwin Ward. It deals with the many-sided survey of the great field of the unsolved problem—the cancer question. The many papers contained in this monograph were presented at the Atlantic City Meeting. They cover heredity and constitutional factors; induction, stimulation and inhibition of tumorous growths; metabolism of cancerous tissues; radiation; and a general discussion of the cancer problem.

Under heredity and constitutional factors, the seven articles all deal with the mouse. In the second subdivision, mainly the chemical aspects resulting from the fact that the sex hormone and carcinogenic agents resemble each other chemically and physiologically, are dwelt upon. The metabolism of cancer tissue deals largely with the effect that cancer has upon the body metabolism.

These short articles with their appended bibliographies are an excellent medium to review the present status of this all important question.

—R. T. Frank.

This volume, *Emotional Adjustment in Marriage*,⁴⁸ has been written to help the physician who may meet in his practice the problems of sexual difficulties in marriage. The various chapters discuss the nature of the sex desire, the deviations, rather than the abnormalities, from what is regarded as normal in this respect, and the assumption of those attitudes and practices in marriage and the sexual relation which are calculated to assist one to the attainment of the greatest possible happiness in such a relation.

⁴⁶*A Manual of Operating Room Procedures*. By Almira W. Hoppe, Science Instructor, Jewish Hospital of St. Louis, and Lucile M. Halverson, supervisor of Operating Rooms, University of Minnesota Hospitals. University of Minnesota Press, Minneapolis, 1937.

⁴⁷*Some Fundamental Aspects of the Cancer Problem*. Symposium Sponsored by the Section on Medical Sciences of the American Association for the Advancement of Science, Atlantic City, New Jersey, December 29, 1936—January 1, 1937. Edited by Henry Baldwin Ward. 248 pages. The Science Press, New York, 1937.

⁴⁸*Emotional Adjustment in Marriage*. By LeMon Clark, M.D., Assistant in Obstetrics and Gynecology, University of Illinois College of Medicine. 264 pages. The C. V. Mosby Company, St. Louis, 1937.

and peripheral respiratory interference. Other factors, as aspiration of débris, and various miscellaneous actions are considered, and there are chapters on cyanosis and anesthetic explosions. In discussing ventricular fibrillation he includes some case reports, and emphasizes the relation of psychic and emotional upheavals. There is a thorough consideration of the use of nitrous-oxide in obstetrics, and the author states that it is safe and desirable *in the hands of a well-trained anesthetist*. The frequent accidents and complications of vomiting during cesarean section is thoroughly discussed, as is also the author's consideration of pre-anesthetic sedatives. The book merits reading by all obstetric operators.

—Philip F. Williams.

The inaugural thesis representing five years of work by Ovidio Unti⁴³ includes both laboratory, animal, and human research with one of the barbiturates "dial." The author would limit its application to basic anesthetics supplemented by inhalation anesthesia. Forty-five human case histories are appended.

—R. T. Frank.

The *Surgical Studies*⁴⁴ written by Ribeiro and published in Brazil, cover a diversity of subjects. In all there are 17 articles. This, in a way, is a report of the surgical activity of the author, dealing with 842 patients on whom 559 major and 283 minor operations were performed, with 9 deaths.

There is an article on 10 cases of nerve lepromata in which surgical intervention was practiced mainly in the caseous stage. Postoperative intestinal paresis is taken up. There are several articles on pyloric hypertrophy in different age groups. Cholecystectomy is advised in conditions of cholecystitis in order to avoid future carcinoma of the gallbladder. The monograph is faultlessly gotten up with numerous illustrations.

—R. T. Frank.

Dr. Brookes has developed in this volume, *Textbook of Surgical Nursing*,⁴⁵ a very thorough and complete exposition of surgical conditions for nurses, and in addition has given a meticulously detailed manual of nursing technic.

In the sections of the book relating to nursing and operative technic he has followed the present set up used in the Barnes Hospital in St. Louis. After discussing the relation of the nurse to the surgical patient, some general surgical principles as inflammation, infection, wounds and tumors are taken up. In a number of following chapters the sequence of material runs through preparation and sterilization, routines of pre- and postoperative care, while the modern anesthetic agents are discussed as to their possible disadvantages or dangers. The author regards cyclopropane and evipol as still in the experimental stage. The three chapters on the operating division might well serve as ground work for organization and also for comparison by established services.

The subject matter of most of the remaining text is devoted to a comprehensive discussion of surgical condition and surgery, of the various systems. Dr. T. S. Brookes has contributed the chapter on orthopedic surgery, Dr. E. A. Graham and Dr. E. Sachs have contributed to the sections on chest surgery and neurologic surgery. Dr. H. S. Crossen has written the chapter on gynecology. The ingenious vaginal operation drape described has merited two full page illustrations, Figs. 36

⁴³Anestesia de base pela Dialilmalonilurea. Thèse Inaugural, apresentada a Faculdade de Medicina do Paraná, 1936.

⁴⁴Estudos Cirurgicos. Enrico Branco Ribeiro, Cirurgião da Beneficencia Portuguesa e do Sanatorio Santa Catharina. São Paulo, Brasil, 1936.

⁴⁵Textbook of Surgical Nursing. By Henry S. Brookes, Jr., M.D., Instructor in Clinical Surgery, Washington University School of Medicine, etc. With 233 illustrations, 636 pages. The C. V. Mosby Company, St. Louis, 1937.

The importance of laboratory tests for syphilis is undoubtedly increasing, and under the impetus of the recently awakened public interest in syphilis, the reliability of such tests will no doubt frequently be questioned. Of interest to physicians then will be this book, *Laboratory Diagnosis of Syphilis*,⁵¹ which by its presentation of the clinical evaluation of the serologic report will be found especially valuable.

The text describes the history of the development of various serologic tests, devotes seven chapters to the Wassermann reaction, four chapters to the flocculation tests and gives a lengthy discussion of the examination of the spinal fluid. Various other tests for syphilis are more briefly taken up.

The section on the clinical evaluation of the serologic reports discusses, especially, the various types of falsely positive reactions. Since in many conditions, as in pregnancy, where syphilis is characterized by a long period of latency, a positive serum is the only objective evidence of the presence of the disease, it behooves the physician to have a definite understanding of the various reports which may be rendered. In discussing cord blood Wassermann reactions, the author states that serologic findings in the cord blood usually reflect the maternal blood findings, and are worthless as a diagnostic test for the presence of syphilitic infection in the newborn. The behavior of the infant's Wassermann taken week after week is, however, regarded as a valuable and frequently the only, clue to such infection. Further it is noted that the reports of the past decade make it reasonably certain that neither pregnancy, anesthesia, nor malignancy predisposes to false positive reactions.

—Philip F. Williams.

Coincident with the recent widespread attempt of the public health organizations of the United States to eradicate syphilis, the appearance of this small book, *Syphilis: The Next Great Plague to Go*,⁵² is timely. Dr. Fishbein, the editor of the *Journal of the American Medical Association*, has prepared this discussion of the disease in his usual inimitable style. The story as he tells it, is complete and explanatory as to the nature, transmission, social and economic aspects of the disease, and of the various methods by which it may be treated and eradicated.

The chapter on the "Prevention of Syphilis in the Prospective Mother and Child" should be read by every obstetrician and married couple, for as Parran has said, "proper oversight of the pregnant woman could eradicate congenital syphilis completely." In the chapter on "When Syphilitics May Marry" the author has included memorandum relating to the legal aspects of the marriage of syphilitics in the various states, and the medical advice given on page fifty-seven insures both parties to the marriage, when one is syphilitic, a square deal.

This book deserves to be read by every adult in the United States.

—Philip F. Williams.

A continued demand for an authoritative textbook on this constantly developing mode of therapy has led Krusen to revise his *Light Therapy*.⁵³ In the general revision of the book fifty-two pages have been added, while the chapter on physiology has been much enlarged. Many new photographs and illustrations have been added.

⁵¹*Laboratory Diagnosis of Syphilis*. By Harry Eagle, M.D., Passed Assistant Surgeon, United States Public Health Service, Washington, D. C., etc. With foreword by J. Earle Moore, M.D., Associate in Medicine, Johns Hopkins University, etc. The C. V. Mosby Company, St. Louis, 1937.

⁵²*Syphilis: The Next Great Plague to Go*. By Morris Fishbein, M.D., Editor, *Journal of the American Medical Association* and of *Hygeia*, the Health Magazine. David McKay Company, Philadelphia, 1937.

⁵³*Light Therapy*. By Frank Hammond Krusen, Associate Professor of Physical Medicine, The Mayo Foundation, University of Minnesota, etc. Second edition, revised, and enlarged. With 42 illustrations, 238 pages. Paul B. Hoeber, Inc., New York, 1937.

The subject of birth control is dwelt upon philosophically, as to its principles and cosmic effect, as well as in a practical manner with a discussion of present available methods and devices. The premarital consultation (Dickinson) is regarded and discussed as an element of preventive medicine.

It is very unlikely that all of the author's views and conclusions will be universally accepted, although a reading of it should be helpful in assisting some physicians to deal with psychic problems in married patients.

—Philip F. Williams.

*Sexual Power*⁴⁹ by Chester Tilton Stone is designed for informing the lay public and the general practitioner. According to the author, less than 50 per cent of civilized men enjoy full sexual potency. In the mind of the average woman, sex is too often associated with hypocrisy and humiliation.

This is a well written and clearly put book covering the subject of potency, impotency (psychic, functional and organic), the psychic and physical basis of sex difficulties as well as the effect of the endocrine glands upon sexual power. I am surprised to see the prostate put among the endocrine glands even if with some reservations. There are such occasional misstatements as—if the anterior lobe of the hypophysis is predominant, masculinization results, if the posterior lobe, feminization, for which statements there is not the slightest proof.

On the whole, this subject is approached from the proper attitude and from the proper point of view. It covers the subject adequately. In my opinion, a number of the brief case histories might well have been omitted without impairing the text.

—R. T. Frank.

This manual on contraception entitled *Marriage and Periodic Abstinence*⁵⁰ is written by J. G. H. Holt who includes among his titles that of "sexologist." Evidently, to this extent, specialization in such matters exists in Holland. He divides the subject matter of intentional birth control into three parts. In the first he deals with the historical aspects of conception and ovulation and then proceeds into the biologic researches coincident with Ogino's discovery. He discusses such objections to Ogino's theory as the proposition that several ovulations may occur in one cycle, that the duration of the cycle may vary under the influence of abnormal circumstances, that the theory is invalid in cycles of from twenty to twenty-two days, and finally, that so-called "violent-ovulation" might be provoked by the sexual act. In discussing the abnormal pathologic conception period, he mentions that we should bear in mind that ovulation is a biologic process and that we cannot control the subtleties of nature. Various symptoms commonly mentioned as suggesting the occurrence of ovulation are described. Detailed rules and directions for practice of the Ogino method are given, but in an intricate and confusing style.

In the second part of the book he discusses the reversal of this method as a therapeutic measure in infertile couples. A general number of test cases with their accompanying menstrual calendars are appended as a third part, and a datometer or calendar measuring device is included with the book. A very full discussion of the intricacies of the method should make the book of interest to those who are engaged in explaining such methods to their patients.

—Philip F. Williams.

⁴⁹*Sexual Power*. By Chester Tilton Stone, M.D., Clinical Assistant Surgeon, Urological Department, Bellevue Hospital, New York, etc. Illustrated, 160 pages. D. Appleton-Century Company, New York, 1937.

⁵⁰*Marriage and Periodic Abstinence*. By J. G. H. Holt, M.D., Gynecologist and Sexologist, The Hague and Harlem, etc. 174 pages. Longmans, Green and Co., New York, 1937.

contributions on the treatment of osteomyelitis. These articles show the type of work that is being performed at the university.

—R. T. Frank.

*Twenty-Five Years of Health Progress*⁵⁷ is a statistical report of 611 pages by Louis I. Dublin and Alfred J. Lotka of the Metropolitan Life Insurance Co. It covers the period of 1911 to 1935 and deals to a great extent with the mortality of those insured in the company. There has been a steady gain in life expectation during this period. This report will interest particularly health officers, physicians, sociologists and life insurance officers.

In the last twenty-five years, the average duration of life has been extended by fourteen years through public hygiene agencies and the advance in medicine. For example, the tuberculosis death rate among the insured has dropped from 242 to 56 per 100,000. There has also been an advance in the standard of living. These statistics represent a huge cross-section of the entire population as there were 17,000,000 weekly paying policyholders in 1935. The main number are composed of urban wage earners.

These statistics should interest the obstetrician and gynecologist greatly as 56 per cent are females while in the general population, females represent only 49.5 per cent. Of the insured, 3,200,000 died, which represent 9.2 of every 1,000 of insured each year.

Of the communicable diseases, tuberculosis, influenza and pneumonia play the greatest rôle. Cancer of the female genitals occurred in 52,700, exceeded only by cancer of the stomach and liver, forming a group of 84,000. In these twenty-five years, there is no evidence of increase of carcinoma of the female genitals.

The puerperal state was responsible for 55,141 deaths. In the general population, the authors add, 375,000 deaths occurred from this same cause. The mortality of puerperal sepsis was 38.5 per cent, puerperal toxemias, albuminuria, 23.1 per cent, all the other puerperal causes which represent sepsis, hemorrhage, etc., 38.5 per cent. There was a decline of 20 per cent in deaths from these causes.

—R. T. Frank.

Annual Report on the Results of Radiotherapy in Cancer of the Uterine Cervix by the *Health Organization of the League of Nations*⁵⁸ is a short statistical pamphlet, the first of a series of annual reports. The committee consists of Dr. J. Heyman of Stockholm, the editor, Dr. Lacassagne of Paris, and Lt.-Col. A. B. Smallman of London.

Future reports are to include analyses of material relating to cancer of the corpus uteri as well as that of the vagina. A report from the University of Brussels of cases treated in 1930 shows the absolute cure rate 14.9 per cent. In the Liverpool Radium Institute there is no absolute cure rate given. From the Marie Curie Hospital in London, the absolute cure rate is 39.4 per cent. From the London Radium Center, it is 15.2 per cent. From the Radium Institute of Paris University no absolute cure rate is offered. From the Radiumhemmet, Stockholm, it is 24.4 per cent.

These tables should prove of increasing value as statistical uniformity is arrived at.

—R. T. Frank.

⁵⁷*Twenty-five Years of Health Progress. A Study of the mortality experience among the Industrial Policyholders of the Metropolitan Life Insurance Company 1911 to 1935. By Louis I. Dublin, Ph.D., and Alfred J. Lotka, D.Sc., with the collaboration of the staff of the Statistical Bureau. 611 pages. Metropolitan Life Insurance Co., New York, 1937.*

⁵⁸*League of Nations Health Organization. Annual Report on the Results of Radiotherapy in Cancer of the Uterine Cervix. First Volume. Statements of Results Obtained in 1930 and Previous Years (collected in 1936). Edited by: J. Heyman, M.D., Stockholm. 74 pages. Columbia University Press, New York City.*

Undoubtedly light therapy will be found beneficial in many general conditions which come under the notice of obstetricians and gynecologists. At present there seems to be no definite indication for its use in most of the specific diseases met in these two specialties.

—Philip F. Williams.

*Medical Morals and Manners*⁵⁴ by Royster contains papers and addresses written or delivered by the author during the last forty years. In one of these papers he says, "No man should be permitted to indulge in reminiscence until he has passed at least beyond the age of fifty years. Before that time usually his outlook is too recent, his experience limited, and his philosophy unseasoned. On the other hand, if he waits until senility overtakes him, his observations may be tinged with maudlin sentiment and hazy forgetfulness."

Many subjects are covered in a simple, attractive way, equally understandable to the medical profession as well as the laity. Medical ethics can be boiled down to the standards of honor and fair dealing with associates and customers. Eighty per cent of the general practitioner's patients are women and therefore he should understand them. He classifies the types of modern doctors into political, business, social, near-quack, the symptom doctor, and the ideal doctor.

Such subjects as athletics and scholarship, physical standards for women, and physical morality are dealt with. He emphasizes that "surgical sense" is of utmost importance and says, "Let us ask to be delivered from the cocksure surgeon. There are many good operators but few good surgeons." A chapter on facts about appendicitis for the laity is included. The book makes pleasant reading.

—R. T. Frank.

These are *Papers from the IV Medical Service of St. Erik's Hospital, Stockholm*.⁵⁵ In this collection of monographs, not only papers from St. Erik's Hospital in Stockholm, but from Hammarsten's Biochemical Laboratory are reported in collaboration. The majority of the articles are in Swedish. Several, however, appear in English.

The papers mainly cover tests applying to kidney function and hematology, as well as some dealing with pancreatic and gastric investigations. One investigation, with a fairly pure secretin, was performed on the human being and this was also used as a test for pancreatic function. Of the articles in Swedish, there is a profusely illustrated one dealing with the glands of internal secretion.

—R. T. Frank.

Volume I of the *Annals of the Faculty of the Medical Sciences of the National University of the Platte*⁵⁶ at Buenos Aires contains many articles by different members of the faculty, both medical and surgical.

There are several communications on diphtheria and its treatment. Likewise one on the serum treatment of erysipelas, an interesting article on tenia saginata, as well as on the distribution of intestinal parasites in Argentine; also one on 2,700 cases of amebiasis, showing how widespread the infestations are in this region.

Of the surgical contributions, the one on ureteral lithiasis, recurrent hydatid in the pouch of Douglas, the etiology of celiac diseases are of interest. Of the technical surgical subjects dealt with is Reichel-Polya gastrectomy for ulcer, two on fractures of the femur, one by the open method, the other by the closed method, and three

⁵⁴*Medical Morals and Manners*. By Hubert Ashley Royster, M.D. 333 pages. Chapel Hill, The University of North Carolina Press, 1937.

⁵⁵*Papers from the IV Medical Service of St. Erik's Hospital, Stockholm*. Edited by Hilding Berglund. 269 pages. Alb. Bonniers Boktryckeri, Stockholm, 1937.

⁵⁶*Anales de la Facultad de Ciencias Medicas de la Plata*. Tomo I. Buenos Aires, 1937.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Collective Review

RECENT LABORATORY TESTS FOR THE EARLY DIAGNOSIS OF PREGNANCY

A CRITICAL REVIEW OF RECENT EXPERIMENTAL WORK

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(From the Department of Gynecology and Obstetrics of the Metropolitan Hospital)

NO TOPIC in obstetrics is receiving more world-wide study at present than diagnostic laboratory tests for early pregnancy. The medical journals are filled with many new and varied tests, and the claims of some authors are at times nothing short of miraculous. These enthusiastic reports have led the average physician to try some of the tests with, in many cases, embarrassing results. So involved have most of us become in trying to sift out the worthy tests from the less valuable and worthless tests that the entire problem has become quite confusing. Prior to 1928 and the advent of the Aschheim-Zondek test, there were some few suggested laboratory methods for diagnosing early pregnancy; i.e., Abderhalden's serodiagnostics test¹ of the protective ferments in pregnancy, and the tests based on glycosuria in pregnancy, which included the phloridzin test of Kammitzer², the glucose tolerance test of Frank and Nothman³ and the adrenalin-glycosuria test of Roubitschek.⁴ These tests were never considered feasible and with the coming of the Aschheim-Zondek test and its remarkable accuracy, these early tests have mostly been forgotten and are herein mentioned only for the sake of academic interest. This paper is an attempt to survey the mass of literature dealing with pregnancy tests in more recent years and to compare the results obtained by different investigators.

ACCEPTED ROUTINE TESTS FOR PREGNANCY

*The Aschheim-Zondek Test.*⁵—This widely known test is now nine years old and employs the use of immature female mice weighing less than 8 gm. and about three weeks of age. Five mice are injected subcutaneously with filtered morning urine of the suspected case three times daily in doses of $\frac{1}{2}$ c.c. each injection; ninety-six hours after the first injection the animals are killed, their abdomens opened, and the ovaries inspected. A positive reaction consists of enlarged hyperemic ovaries with small pinpoint blood spots dotting the surface. These are corpora hemorrhagica. The presence of corpora lutea makes the diagnosis even more conclusive. This specific ovarian stimulation is due to the presence of large amounts of anterior pituitary-like hormone which is found in the urine of early pregnancy. In 2,000 cases tested by this method by Aschheim,⁶ he obtained 98 per cent correct positive reactions and 99.5 per cent correct negative reactions. Other investigators (eleven independent groups reported by Mazer and Goldstein⁷) using the same tech-

This book, *Mortality Trends in the State of Minnesota*,⁵⁹ by Calvin F. Schmid, brings together in compact form significant statistical data regarding mortality in that state and should be of interest to those of the medical and allied professions who are concerned in public health problems. The study covers the mortality experience of Minnesota from 1910 to 1935, and demonstrates that during this period of twenty-six years the general mortality rate has fallen from 11.2 to 8.2. The minimum rates approximate the period of economic depression which began in 1929. The author speculates on the causative factors.

The trends in the principal causes of death for the period are discussed, and the more important causes are considered in detailed form for the biennial period of 1932 and 1933. Here it has noted that cancer of the uterus accounted for 7.2 per cent of the cancer deaths, in other words this condition holds fifth place with 934 deaths.

During this biennium premature birth with 1476 deaths, held seventh place. Injuries at births, with 499 deaths, held seventeenth place. Diseases of pregnancy, childbirth, and the puerperal conditions, with 416 deaths, ranked in twentieth place. Because of the stigma attached to the certification of deaths from syphilis, it is recognized that the death rate from this cause cannot be considered reliable.

Mortality is also discussed from the standpoint of age and sex, as are also the mortality trends. The expectation of life at birth for females in Minnesota is given as 65.2 years. The excess of mortality among wives for the younger ages is ascribed mainly to the hazards of childbearing. Eighty-five per cent of the deaths attributed to gonococcal infection were in females. One-third of all cancer deaths, uterus and other female genital organs, were in women of sixty-five years of age, and there were only three such deaths recorded under thirty years of age.

Infant mortality rate in Minnesota has undergone a significant and continuous decline. Among the factors contributing to this downward movement has been the definite program for infant welfare, which includes the education and prenatal care of expectant mothers. The birth rate in Minnesota is dropping. The number of stillbirths in Minnesota has remained practically stationary. There has been a slight decline in the maternal mortality rate in Minnesota during the twenty-six-year period with two high peaks shown in the post-influenza years. A minimum maternal mortality rate of 4.3 per 1000 live births was recorded in 1929. Puerperal septicemia was followed in order by toxemia of pregnancy, hemorrhages of pregnancy, and other accidents, as the most frequent causes of the puerperal state.

Other chapters deal with the seasonal variations of mortality, and with comparative statistics regarding maternal mortality, and other causes of death in the registration area of the United States.

—Philip F. Williams.

*Intimate Side of a Woman's Life*⁶⁰ is the suggestive and for this reason somewhat objectionable title of a most useful small volume by Leona W. Chalmers. After a brief and correct description of the pelvic organs the author speaks of constipation, leucorrhea, contraception and general body hygiene. The specific value of this book lies in the intelligent form in which such common procedures as enemas, vaginal douches, certain exercises, etc., are described. In referring his patients to this book the physician will save much time and know that these procedures will be carried out in a proper manner.

—Hugo Ehrenfest.

⁵⁹*Mortality Trends in the State of Minnesota*. By Calvin F. Schmid, Assistant Professor of Sociology, University of Minnesota. 317 pages. The University of Minnesota Press, Minneapolis, 1937.

⁶⁰*Intimate Side of a Woman's Life*. By Leona W. Chalmers. Illustrated, 128 pages. Pioneer Publications, Inc. Radio City, N. Y., 1937.

the gross error to be 3.9 per cent and a corrected error of 1.8 per cent. Goldberger, Salmon and Frank²³ performed duplicate tests on 1,093 pregnant women and found only 0.55 per cent false negatives and 0.09 per cent false positives. Feresten, in 1937, using a modified Friedman technique²⁴ tested 1,600 unknown urines with a total error of 0.94 per cent.

Kelly and Woods²⁵ recently gave many details and finer points in the technique of the rabbit test which when adhered to undoubtedly make the percentage of error even smaller. Evans, Kohls and Wonder²⁶ presented a new graphic curve of anterior pituitary-like hormone output in pregnancy, showing a maximum in the first trimester of pregnancy. Their work gives a satisfactory explanation for the accurate results obtained so early in pregnancy by the Aschheim-Zondek and Friedman tests. Schwarcz²⁷ suggested the use of blood plasma instead of urine in the Friedman test and reported excellent results in a small series of cases. His work requires further study.

Comparison of the Aschheim-Zondek and Friedman Tests: Many laboratory workers adhere to one or the other of the two tests, and it is simply a question as to which test one is accustomed. Aschheim and his followers maintain that the mice are infallible while Friedman and his supporters claim that the rabbit is more advantageous because the test is quicker, more economical and the rabbit is less easily killed by toxic substances and less bothersome as a test animal.

In summarizing the comparative value of the two tests Crew²⁸ states that both the Aschheim-Zondek and the Friedman tests are 99 per cent perfect. Crew maintains that "a 90 to 95 per cent accuracy is not sufficient. . . . No test which yields more than 1 per cent of error can claim much support." Dawson²⁹ finds the mouse and the rabbit tests 99 per cent correct and positive within fourteen days after conception. Mack and Agnew compared the two tests in 1,110 cases and found them equally exact. As more refined techniques are being introduced the personal error in each case will eventually dwindle and both tests at some future date should prove 100 per cent accurate in trained hands.

GONADOTROPIC HORMONE TESTS USING MALE RODENTS

*The Brouha Test.*³⁰—Brouha and his associates used immature male mice and injected them in a manner similar to the Aschheim-Zondek technique. The test is based on an increase in size of the seminal vesicles in the male mouse after being subjected to pregnancy urine stimulation. Brouha reported a small series of cases, in which however, he had obtained excellent results. White and Severance³¹ encountered 10 false positives in a series of 27 nonpregnant women. If this test can be proved to be accurate in a large series of cases it would be of great value.

*The Zaharesco Test.*³²—Zaharesco-Karaman and his associates more recently reported a test for pregnancy which is a variation of the Brouha test. Rats are injected daily with 1 c.c. of blood or urine of pregnancy and after seven to ten days the animals are killed and a ratio is taken between the weight of the seminal vesicles in mg. and the weight of the rat in grams. If the ratio is more than 1 the reaction is considered positive. This test can in no way hope to supplant any of the accepted tests since seven to ten days are required before the reaction can be read. The computations are much more involved and complicated than even in Brouha's test.

THE ESTRIN TESTS FOR PREGNANCY

*The Mazer-Hoffman Test.*³³—This diagnostic test is based on the presence in the urine of pregnancy of large amounts of estrogenic substances which produce when injected into immature or castrated mice or rats an epithelial desquamation in the

nique or some slight variation, performed the tests on 2,807 cases and obtained on the average, correct positives in 94 per cent and correct negatives in 97 per cent of the cases. More recently Mack and Agnew⁸ reported the work of 19 other investigators who tested 8,685 cases with the Aschheim-Zondek test and found an average accuracy of 96.6 per cent. In 1935 Aschheim mentioned⁶ that up to 1933, investigators who worked with this test reported 11,345 urine examinations with only 1.8 per cent false results.

It thus is evident that the Aschheim-Zondek test is a most valuable addition to the armamentarium of the physician and laboratory worker. Recently Davy and Sevringhaus⁹ using slight variations of the Aschheim-Zondek technique in undiagnosed and borderline cases, managed to obtain 90 per cent correct results when one test was used alone and much better results when a correlation of two-methods was put in use. Other investigators employed rats in the test and Reiprich¹⁰ found that rats are more sensitive and more rapid in reaction than mice, since injections of 10 to 25 c.c. of urine into immature rats could be tolerated, and the reaction could be determined in from twenty-four to thirty-six hours. According to Reiprich a positive reaction in immature rats consists in hyperemia and hypertrophy of the ovaries to 3 or 4 times the size of the immature ovaries. More recently Mull and Underwood¹¹ tested 702 urine specimens by injecting immature rats with 2 c.c. of urine daily for five days and killed the animals on the sixth day. Working under suboptimal conditions their results were 91 per cent accurate, which upon consideration of the obstacles imposed were remarkably good. The possibility of the rat taking the place of the mouse as a pregnancy indicator is not a likely one, but in many cases where the urine has proved too toxic for the small mouse, the larger animal might be used to good advantage.

Sar-Louis¹² performs the Aschheim-Zondek test with mature mice and points out a difference in response of the mature animals to urine of pregnant or nonpregnant women. The difference, however, is not very striking and his suggested variation does not look very promising.

*The Friedman Test.*¹³—This test, originated soon after the Aschheim-Zondek test, represents a simple modification, employing female rabbits, kept isolated, instead of mice. According to the original technique of Friedman (of which today there are many modifications) the rabbit is given 6 intravenous injections of urine in 4 c.c. doses during forty-eight hours, after which the animal is killed and the ovaries examined. Variations of the technique include a single injection of 15 c.c. of urine or a 10 c.c. injection on each of two days. Formerly the animal was killed and thus used for only one test, but it actually can be used a few times by opening the animal dorsally and replacing the ovaries each time after inspection. The results obtained by Friedman and Lapham,¹³ in their original paper, were 100 per cent correct positives and negatives. A comparison of later reports by Mazer and Goldstein⁷ shows that up to 1932 six independent workers obtained 99 per cent correct negative and 96 per cent correct positive results in 535 cases with the rabbit test. Up to 1933 Mack and Agnew report a 98.5 per cent accuracy obtained by 15 different and independent authors who tested 1,899 cases. Ware and Main¹⁴ reported 99 per cent accuracy in 100 cases, and Young, in 1934, recorded the same degree of accuracy in 350 cases.¹⁵ Spielman¹⁶ performed 635 Friedman tests and maintained that the test "warrants universal adoption." Sharp¹⁷ in New Zealand found the test 98 per cent correct, and recently Gernez,¹⁸ Borrás,¹⁹ and Lejwa and Fryszberg,²⁰ found the test almost 100 per cent correct.

Best and McHenry²¹ used two rabbits for each test and out of 538 tested urines obtained 251 positive reactions with 1.6 per cent error and 287 correct negatives with 2.1 per cent error. King²² reviewed the literature and with 4,500 rabbit tests found

FROG TESTS FOR PREGNANCY

The South African Frog, Xenopus Laevis.—Shapiro and Zwarenstein,⁴⁹ in 1935, used a frog as a pregnancy indicator and found that out of 132 tests, 64 checked correctly in pregnant, and 68 checked correctly in nonpregnant individuals. The test consists of an injection of a prepared urine of pregnancy, followed by stimulation of the reproductive cycle in from six to twelve hours. In the South African female, claw-toed frog, after the injection the eggs are found in the cloaca, or if the reaction is not so strong they are found in the oviducts. This test is excellent and the error is practically negligible. The only drawbacks, which are very important ones, are that the frogs are obtainable only in South Africa and become useless after one month, thus necessitating a continuous fresh supply.

Frog Melanophore Reaction.—Konsulov⁵⁰ used hypophysectomized frogs (*Rana esculenta*) and injected 2½ c.c. of urine into the lymph sac of the frog. Pregnancy urine causes the skin of the frog to darken in 1 to 2 hours. Bruhl and Rieckhoff,⁵¹ in 1935, repeated the Konsulov reaction in which pigment reappears in hypophysectomized frogs after the urine injection, and found that the test was not accurate unless the urine was concentrated eight times in volume. However, they found that other conditions besides pregnancy caused the darkening of color. Four cases of carcinoma and one out of three cases of tuberculosis and one case of gonorrhea gave the reaction. The melanophore test cannot be recommended until further work is done. Stabilization of certain factors might lead to a valuable test for pregnancy.

ALLERGIC SKIN TESTS FOR PREGNANCY

The Gruskin intradermal test for pregnancy.

The intradermal anterior pituitary-like hormone test of Gilfillen and Gregg.

Gruskin Intradermal Test for Pregnancy.—In 1936 Gruskin⁵² reported excellent results with a simple intradermal pregnancy test. All that is necessary is to inject intracutaneously a few minims of an especially prepared placental extract. In ten minutes the diagnosis of pregnancy could be established or disproved by the presence or absence of a local erythematous reaction with pseudopodia. Gruskin explained the manifestation on an allergic basis, and suggested the possibility of production of a new protein-like substance by the placenta which is foreign to the nonpregnant woman. More recently Schwartz⁵³ repeated Gruskin's work and obtained 96 per cent correct positives in 155 cases and 90 per cent correct negative reactions in 66 cases. These results appear at first glance to be fairly good, with so simple a test. However, the test is not applicable to various types of cases. Women with disturbances in metabolism, with endocrine and skin abnormalities, and allergic individuals who are sensitive to many types of proteins will undoubtedly show false reactions with such a skin test. Schwartz, himself, mentioned other limitations of the test. "A thorough knowledge of the fundamentals of wheal formation is essential to any one who expects to employ skin testing extensively." The personal error in interpreting the different types of reactions and the individual reactions of susceptible patients make this test useful only in the hands of a specialist in allergy. Perhaps with further study and standardization this test can be made useful to the average practitioner. If Dr. Schwartz himself reports six cases as erroneously positive out of 60 nonpregnant women, there still remains much more investigation to be done before the average physician could adopt this test.

The Intradermal Anterior Pituitary-like Hormone Test.—Gilfillen and Gregg⁵⁴ recently reported another intradermal test claiming that it is even more sensitive than the Aschheim-Zondek test in certain borderline cases. An injection of a few minims of antuitrin-S intradermally produces a wheal and redness in nonpregnant females under thirty years of age. In the pregnancy cases, no skin reaction is noticeable

vagina characteristic of estrus. The test runs for ninety-six hours and vaginal smears are taken daily. The results obtained by Mazer,³³ and Bland³⁴ show that the test is a poor diagnostic test for pregnancy, since it yields only 75 per cent correct positives. However, the correct negatives in nonpregnant women are 97 per cent accurate. This test is then worth far more as a test for ruling out pregnancy than for actually establishing the diagnosis of pregnancy.

*The Kelly Test.*³⁵—Kelly introduced a simple variation of the estrin test by merely observing the extent of patency of the vaginal orifice of albino rats. After an intraperitoneal injection of 5 to 15 c.c. of pregnancy urine, a premature opening of the vaginal canal in from seventy-two to eighty-four hours is considered diagnostic for pregnancy. Hulpieu, Weatherby and Culbertson found³⁶ that the Kelly test is not better than the Friedman test; that it takes double the time, has a high mortality rate, and in the 59 cases tested gave more false positives than the Friedman test. However, Kelly's observation should be kept in mind when performing the routine Aschheim-Zondek test as it may serve as a corroborative test before the ovaries are inspected.

FISH TESTS FOR PREGNANCY

The Female Bitterling Test.—There have been many tests for early pregnancy suggested by using fish as the laboratory animals but none of these have shown much worth. Fleischmann and Kann, in 1932,³⁷ first described the lengthening of the ovipositor of the female bitterling as a diagnostic test for pregnancy. The fish which normally is found in the rivers of central Europe possesses an external egg-laying tube, the ovipositor. During normal breeding season, the female extrudes the ovipositor and allows the ova to drop out and be fertilized. Fleischmann and Kann procured this elongation at will by merely adding urine of pregnancy to the water in the tank. Szusz,³⁸ in 1933, showed that this test was not specific for pregnancy. Kanter, Bauer, and Klawans,³⁹ more than a year after Szusz had completed his work, compared this fish test with the Aschheim-Zondek test and obtained exceedingly promising results. They suggested its use anew as an indicator of pregnancy. Owen⁴⁰ repeated the tests with the female bitterling and also thought it to be a good test for pregnancy notwithstanding the fact that his results were only 75 per cent accurate. Kleiner, Weisman and Barowsky repeated the work of Szusz but demonstrated that the so-called pregnancy reaction could be brought about as well by male urine, urine from postmenopausal women and nonpregnant single girls.⁴¹ This observation was supported by Glaser and Haempel⁴² Kotz, Douglas, and Parker,⁴³ Gottlieb,⁴⁴ and Moses.⁴⁵ The female bitterling test has since been shown by Kleiner, Weisman, and Mishkind⁴⁶ to be due to the presence of the male sex hormones and substances of closely related structural formulas.

The Male Bitterling Test (Coloration Test).—The male bitterling has been used by Tozawa⁴⁷ as a diagnostic animal for pregnancy determination, on the basis of a change in its color when urine of pregnancy is added to the fish in the aquarium. The attainment of the reddish coloration is neither exact nor has it been found of scientific value, since the personal error in differentiating between positive and negative readings is too great.

The Stichling Melanophore Reaction.—Mandelstamm⁴⁸ showed that a species of fish known as the Stichling underwent a darkening in color after being exposed to pregnancy urine for only two hours. Scant data were given by the author and only a 75 per cent accuracy was reported. The use of fish as experimental laboratory animals in the field of sex hormones is only recent, yet the rapid physiologic change which takes place in these cold blooded animals may in the very near future, open a vast field in the "scarcely touched-upon world" of the sex hormones.

out of 26 cases. Though acceptable the Kapeller-Adler reaction was not sufficiently accurate to displace the Aschheim-Zondek test.

In 1936, Gertlers⁸¹ demonstrated the presence of histidine in the urine of more than 90 per cent of gravid women, but the reaction often became positive only in the later months of pregnancy. Kriegers⁸² reviewed the different modifications of the bromine water test, and agreed with Seidman that the histidine test is valueless as a means of detecting early pregnancy. An editorial in the *Journal of the American Medical Association* (June 27, 1936)⁸³ summarizes: "Further data must be secured in order to determine definitely whether this relatively simple chemical test for urinary histidine may be of at least of some value in the clinical diagnosis of pregnancy."

The Visscher-Bowman Test.—Visscher and Bowman,⁸⁴ in 1934, devised a new and rather complicated chemical test for pregnancy, which involves the use of many chemical ingredients with a rather muddled and lazy reaction. The original test consisted in the addition of one drop of hydrogen peroxide, five drops of 1 per cent phenylhydrazine-HCl solution in water, five drops of methyl cyanide solution in water, and five drops of concentrated hydrochloric acid to 1 c.c. of urine. The mixture is heated on a water-bath for twenty-five minutes. A russet color and a thick flocculent precipitate denote a strong positive reaction, indicating pregnancy. A brown color and a slight powdery precipitate a doubtful reaction. No color change and no precipitate denotes a negative pregnancy test. Visscher and Bowman reported 93 per cent accuracy in pregnancy cases. In the same year Menken⁸⁵ used two different techniques of the test and obtained good results. Later Menken repeated the test on another series⁸⁶ and came to the conclusion that a definitely positive test is reliable as proving pregnancy, but that a negative test does not mean the absence of pregnancy. In 1936, Dodds⁸⁷ tested 100 cases and obtained a 90 per cent accuracy with pregnant women and 89 per cent exactness with nonpregnant women. Dolff⁸⁸ also reported good results with this test, finding the test 94.5 per cent accurate in early pregnancy, and 96 per cent accurate in later pregnancy. However, Dolff found that urines were also positive when they contained excessive amounts of the decomposition products of metabolism. Friedrich⁸⁹ stated that the gonad-stimulating hormone is the causative factor and he greatly simplified the Visscher-Bowman technique. Friedrich's technique consists of the simple addition of a few drops of 25 per cent HCl to 1 c.c. of urine which is at the sp. gr. of 1.015. The mixture is heated over a Bunsen burner for two minutes when a color change takes place. A light brown coloration is a negative reaction, and a dark or red brown color is a positive reaction. Friedrich tested 312 cases both with his method and with the original Visscher-Bowman technique. Only five wrong results were obtained with the Visscher-Bowman method, while the hydrochloric acid method of Friedrich gave 100 per cent correct results. Simple addition of HCl to urine certainly would be a convenient indicator of pregnancy. Frech,⁹⁰ in 1937, repeated the original Visscher-Bowman test in a series of 513 cases and obtained 92.3 per cent accuracy in diagnosing pregnancies. Frech stated that this test "requires considerable experience in learning to differentiate the various precipitates obtained. It is often difficult to differentiate between a flocculent and a powdery precipitate. The test is positive if a reddish-brown flocculent precipitate is observed;—if straw yellow and the deposit is powdery or absent, it is negative." Frech continues by adding that "in 15 cases checked by Aschheim-Zondek tests only 80 per cent correct results were obtained."

Incidentally, it should be kept in mind that urine contains many substances. John F. Loehle⁹¹ reported very recently that both male and female urines containing sugar, have given a positive Visscher-Bowman reaction. We maintain that any test which is not specific for pregnancy requires particular investigation.

The Colorimetric Test of Schmulowitz and Wylie.—In 1925 Schmulowitz and Wylie⁹² devised the following pregnancy test: The estrin extracted from urine by

after injection. This same test previously had been performed by Porges and Pollaczek,⁵⁵ and by Deutsch,⁵⁶ and Strauss.⁵⁷ All three investigators were convinced that the anterior pituitary hormone test was not accurate enough for pregnancy diagnosis. Recently the *Journal of the American Medical Association*, on two different occasions,^{58, 59} did not lend its support to this intradermal test, due to its inaccuracy. Weisman and Yerbury⁶⁰ were the first to show that even with the identical commercial product and the same technique, used by Gilfillen and Gregg, the test was valueless. Later, Schneider and Cohen⁶¹ repeated the test on a larger series of cases and corroborated the findings of Weisman and Yerbury. They concluded: "The results obtained with antuitrin-S injected intradermally in no way exhibit the reliability of this test as a means of diagnosing pregnancy or gynecologic disorders." Further work is required to establish a practical value of this intradermal test.

CHEMICAL TESTS FOR PREGNANCY

The Urinary Histidine test.

The Visscher-Bowman Test.

The Colorimetric test of Schmulowitz and Wylie.

The Urinary Histidine Test for Pregnancy.—Voge⁶² using Knoop's bromine water test for histidine, evolved a test for pregnancy based on the finding of histidine, an aminoacid, in the urine of pregnant women. He boiled such urine with dilute bromine water and noted the pink color change. In a series of 60 cases controlled with Aschheim-Zondek test he found this test 95 per cent accurate.

Armstrong and Walker⁶³ isolated histidine from pregnancy urine and demonstrated that the presence of this aminoacid in the urine accounted for the positive bromine water test of Voge. The exceptionally good results obtained by Voge with so simple a test, stimulated several investigators to study this reaction. Dodds,⁶⁴ Siddall and others,⁶⁵ and Pellizzari⁶⁶ were among the first to repeat this work and irregular results were obtained by each group. Pellizzari found histidine present also in nonpregnant women and declared the test as valueless.

Kapeller-Adler and her associates^{67, 68, 69} studied the reaction in great detail, suggested a modification for quantitative histidine determination in urine and claimed excellent results with this new test. In the meantime, Young⁷⁰ using the original Voge bromine water test obtained but 63 per cent correct positive reactions and 84 per cent correct negatives. He concluded that this was not a satisfactory test for pregnancy. In 1933 Weisman also used Voge's test and found irregular positive and negative reactions in a series of definitely known late pregnancy cases.⁷¹ Valle,⁷² in 1934, used the Kapeller-Adler modified histidine test and found it correct in 98 per cent of his cases, starting at the second month of gestation. Valle performed the test in thirty minutes and his work appeared to be quite promising. Weiss⁷³ concluded, after investigations into the histidine test, that a definite, positive histidine test was diagnostic of pregnancy. Ohligmacher⁷⁴ used the Kapeller-Adler modification of Voge's test and found it no better than the original test! He considered it neither sensitive nor specific. In 1934, Ferrari and Francis⁷⁵ of Buenos Aires performed the Kapeller-Adler test and reported it as valueless. However, at about the same time Renton,⁷⁶ in South Africa, did 100 tests with the Kapeller-Adler reaction and had only seven false negatives. Brandsch,⁷⁷ in Leipzig, found 19 per cent incorrect reactions in early pregnancy and 9 per cent incorrect reactions in late pregnancy. In his opinion the metabolism of histidine is very interesting, though histidine may be present in the urine of nonpregnant females. Foldes⁷⁸ obtained poor results with the Kapeller-Adler test but Seidman,⁷⁹ in 1935, stated that the histidine test warranted further study because he was not satisfied as to its specificity for pregnancy. Hecksteden⁸⁰ maintained that the Kapeller-Adler reaction was useful, reporting 64 correct positives out of 75 cases tested; and 21 correct negatives

is no definite explanation for the pupillary change and in many cases of known pregnancy there is neither a dilatation nor a contraction of the pupil. The error in the ophthalmic test is far too great to permit its clinical usage.

The Human Vaginal Biopsy Test.—Very recently Smith and Brunner¹⁰⁰ developed a histologic method for the early diagnosis of pregnancy. Sections from vaginal biopsy specimens are studied microscopically. They reported 79 cases; in 26 of them pathologic changes, e.g., due to vaginitis, etc., rendered the specimens useless. The test is therefore hardly a practical one.

The Contractile Uterine Test.—Still used by some practitioners in Europe is the test first proposed by Lorrincz, in 1928, and investigated by Reeb in 1932.¹⁰¹ A sterile solution of posterior pituitary extract is injected into the woman intravenously. The examiner then performs a bimanual palpation. If the woman is pregnant uterine contractions are felt, and in the absence of palpable contractions the patient is considered not pregnant. Reeb advocated this test after diagnosing correctly 5 pregnant and three nonpregnant women, in a series of eight. He cautions against use of this test in late pregnancy but asserts its value in early diagnosis. In my opinion it is too risky for use in any month of pregnancy.

Pregnancy Diagnosis by Leucocyte Count.—De Nito¹⁰² recently described a new, rapid method for the early diagnosis of pregnancy. This test is founded on diminution of the leucocytes in the blood of the rabbit after an injection of pregnancy urine. After determination of the rabbit's leucocyte count, 5 to 10 c.c. of urine from the suspected case are injected into the marginal vein of the rabbit's ear. The positive diagnosis of pregnancy depends upon a reduction of leucocytes in from two to four minutes after injection. De Nito obtained in 100 cases a 90 per cent accuracy. The author offers no rationale for the reaction, yet the results and the simplicity of the test warrant further investigation.

The Chamorro Modification of the Friedman Test.—Chamorro removed both ovaries from the abdomen of the rabbit and implanted them into the anterior chambers of the same rabbit's eyes. The transplanted ovaries respond in the same manner as ovaries in the Friedman test. The response is slower but available for direct observation. The author performed this test on only a small series of cases and as yet has insufficient data upon which to judge the dependability of such a test.¹⁰³

Infusorial Test for Pregnancy.—Kustallow recently used various protozoa in a method for detecting pregnancy.¹⁰⁴ His test consists of the addition of one drop of catheterized urine to one drop of hay infusion containing various protozoa. In case of pregnancy the motion of these organisms is stopped in less than two minutes. Normal urines do not interfere with their movements. Infections of the urinary tract delay the reaction. No percentages of accuracy are given by the author.

Hoffmann Seed Test.—Hoffmann¹⁰⁵ found that pregnancy urines inhibit the sprouting of seeds. However, after sprouting has started, pregnancy stimulates the growth much more than normal urine. The results are very vague.

Guinea Pig Test.—Gismondi and Acevedo¹⁰⁶ repeated the work of Joel and Andreani Constantin using male guinea pigs one month of age. Two cubic centimeters of pregnancy urine were injected into the heart of the guinea pig and in forty-eight hours hypertrophy of the sexual organs was observed. The results were not found to be reliable.

SUMMARY

A review of the most recent work in pregnancy testing is presented. The Aschheim-Zondek and Friedman Tests both only seven or eight years old have been established as accepted universal tests for pregnancy. As time passes the slight percentages of error in these tests are growing less and less. Other tests are pre-

ether is coupled with diazotized para-nitro aniline which gives a color reaction. This color is compared in a colorimeter with a 33 per cent ferric chloride solution. The more intense the estrin color the more hormone is present in the urine. The above investigators have established an arbitrary number above which the pregnancy diagnosis is positive and below which it is negative. They claim excellent results for this test. Pincus and others⁹³ also advocated a colorimetric method to diagnose pregnancy by estrogens in urine. They varied the Schmulowitz-Wylie test by using phenolsulfonic acid. Pincus and others concluded that the colorimeter test based on estrin in urine is not a reliable test in the early months of pregnancy, but very accurate in the later months of gestation, due to an increase in the urinary estrogen as pregnancy advances.

Realizing the apparent value of the colorimetric test in the last trimester of pregnancy, Savage and Wylie⁹⁴ have ingeniously applied the colorimetric test to the diagnosis of toxemias late in pregnancy. In testing nephritic and preeclamptic toxemias of pregnancy they found a diminished amount of estrin in the urine of those cases, with a corresponding "Ferric Number" (F. N.) of low value (ferric number 37-50) while in the normal average pregnancy the ferric number is about 80. However, there is a large percentage of error since 30 per cent of the normal readings are sufficiently low to overlap those of the toxemia readings. This fact warrants further investigation.

MISCELLANEOUS TESTS FOR PREGNANCY

The following tests are presented purely for the sake of academic interest and completeness. These tests are still in the experimental stages and while some are based on sound physiologic principles, others are simply observations of interesting phenomena.

Hormonal hypercholesterolemia as test for pregnancy

The Bercovitz ophthalmic test

The human vaginal biopsy test for pregnancy

The contractile uterine test of Lorrincez

Pregnancy diagnosis by leucocyte count

The Chamorro-Friedman rabbit test

Infusorial test for pregnancy

Hoffmann seed test for pregnancy

Guinea pig test

Hormonal Hypercholesterolemia.—Masciottra and Martinez de Hoz in 1933⁹⁵ found that upon injecting pregnant urine into guinea pigs, the cholesterol value increased from 30 to 50 per cent. They considered this a diagnostic test for pregnancy and any increase in cholesterol over 25 per cent was believed to be a positive test. This work was repeated by De Potter⁹⁶ but the cholesterol values were found to be so inconsistent, as to be of no clinical value. Gavioli in Buenos Aires⁹⁷ also investigated this test and found cholesterol values of no worth in the diagnosis of pregnancy.

The Bercovitz Ophthalmic Test.—In 1930 Bercovitz⁹⁸ made the observation that a partial mydriosis or myosis would take place in the pupil of a pregnant woman if a few drops of her serum or citrated blood were instilled into the corner of her eyes. This reaction took place in two minutes and according to Bercovitz with 84.7 per cent accuracy. Pouliot used this test and with minor changes in illumination diagnosed 44 cases correctly. Davis, Konikov and Walker used this observation of pupillary changes when performing routine Friedman tests upon rabbits, and could determine the diagnosis of pregnancy by the pupils of the rabbit even before the rabbits were opened for inspection of the ovaries.⁹⁹ Their results were 87 per cent correct positives with a 14 per cent error in nonpregnant individuals. There

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Selected Abstracts

Complications of Pregnancy With Disease

Goodall, J. R., and Gottlieb, Rudolf: The Association of Pregnancy, Hypochromic Anemia and Achlorhydria, Canad. M. A. J. 35: 50, 1936.

It is known that hypochromic anemia is confined principally to women of middle age and is characterized by pallor, weakness, brittle finger nails, achlorhydria, and an anemia with a lowered hemoglobin content without a corresponding diminution in red blood cells. The onset is insidious.

This series consists of 200 consecutive unselected pregnancies. Only average figures are given. The general average hemoglobin was 75 per cent or 10.5 gm. The first, second, and third trimester averages are 80 per cent (11.2 gm.), 75 per cent (10.5 gm.), and 65 per cent (9.1 gm.), respectively. The red blood cell count shows a decrease for the three trimesters from 4,300,000 to 4,100,000 to 3,700,000, respectively. Only 115 had gastric analyses with 51 per cent, 13 per cent, and 0.5 per cent normal gastric acidity for the respective trimesters. In 85 per cent of the above group acidity began to return within a week postpartum.

There is a definite tendency in pregnancy to the development of a progressive hypochromic anemia and it is more pronounced when the succeeding pregnancies are in rapid order.

The authors feel that the fetus draws upon the maternal source for gastric factor as well as supply of iron. They suggest that the primary cause of hypochromic anemia and its associated lesions is due to an endocrine dysfunction.

Large doses of ferrous carbonate have given satisfying results.

H. CLOSE HESSELTINE.

sented some of which show promise and others of which are practically worthless. The goal of the investigator is to discover a reliable test for pregnancy which can be performed in a test tube in a few minutes. To that end we can but look to the future.

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the postpartum period. The blood sugar test, therefore, becomes of diagnostic importance. Dietetic treatment in the face of a high blood sugar may serve to divert subsequent disaster.

The authors conclude that the incidence of toxemia was much lower in the iron-treated series than in the controls. When the hemoglobin value is kept up about 90 per cent, the incidence of toxemia is lowered.

F. L. ADAIR AND S. A. PEARL.

Boycott, John A.: Anaemia in Pregnancy, Lancet 1: 1165, 1936.

The author supplies an excellent review of the literature and converts the various results to a common system, thus enabling the reader to follow the comparisons easily. In the study of 222 cases the following technic was employed: hemoglobin estimations are made by the Haldane hemoglobinometer standardized at an oxygen capacity of 18.5 c.cm. per cent, equivalent to 13.8 gm. hemoglobin; red cells are counted by dilution with physiological saline solution in a Bürker chamber; cell diameters are measured by the Price-Jones method; films are fixed and stained in Jenner and counterstained with 0.5 per cent aqueous eosin; and reticulocytes are counted by a wet method.

Anemia is limited to that group having less than 80 per cent hemoglobin.

Evidence is obtained to show that there is an inconsistent increase in the plasma volume in pregnancy causing a dilution of the red cells. Anemias may result from iron deficiency through demands of the fetus and either dietary insufficiency or defective utilization of iron. The other anemias of pregnancy may result from complicating diseases; the majority of these are of the hypochromic type.

Twenty-two per cent of the patients attending the University College Hospital Antenatal Clinic have less than 80 per cent hemoglobin. True anemias may be distinguished from the apparent (dilution) anemias by the blood picture, yet these may coexist. It is stated that anemia is probably not a serious risk in pregnancy in England and that the common anemia of pregnancy responds well to adequate iron treatment unless there is a complicating disease.

H. CLOSE HESSELTINE.

Bentivoglio, Franco: Chronic Myeloid Leukemia Associated With Pregnancy, Folia gynaecc-demograph. (Genova) 33: 53, 1936.

The author briefly describes a case of chronic myeloid leukemia associated with pregnancy and treated by x-ray therapy. During the course of pregnancy there was noted no change for the worse in the leukemia, if anything there was some improvement of the condition.

The pregnancy terminated spontaneously, with the birth of a live child, which had no symptoms of the disease.

MARIO A. CASTALLO.

Daniachij, M. A.: Pathological Pregnancy and Hematopoiesis, Zentralbl. f. Gynäk. 60: 1998, 1936.

Daniachij studied the hematopoiesis of bone marrow in relation to the various pathologic forms of pregnancy with special reference to the toxemias of pregnancy.

In general he found that hematopoiesis in the anemias of pregnancy is markedly suppressed due to the general toxic state of the patient. In studying his case material he found that pregnancy may be considered as being the most important etiologic factor of the various forms of anemia including Edison-Biermer's pernicious anemia.

Smallwood, W. Carey: *The Anaemia of Pregnancy*, Brit. M. J. 2: 573, 1936.

The author presents a classification of the disease based on other recent classifications of blood dyscrasias. He concludes that there exist mild degrees of hypochromic anemia of pregnancy which, though not dangerous to life, are responsible for minor ailments and ill-health in both mother and child and may be prevented or cured by a generous diet and the administration of iron. Occasionally, severe degrees of anemia develop during and as a result of pregnancy in the last trimester.

These conditions require detailed blood studies, accurate diagnosis and prompt treatment directed toward the type of anemia present. A routine hemoglobin estimation at about the seventh month of pregnancy and a detailed hematologic analysis of all cases showing severe degrees of anemia should form part of antenatal supervision.

F. L. ADAIR AND S. A. PEARL.

Fullerton, Harold W.: *Hypochromic Anaemias of Pregnancy and the Puerperium*, Brit. M. J. 2: 577, 1936.

The author presents a study of hypochromic anemia occurring during pregnancy and the puerperium. The average hemoglobin levels of poor women fell during pregnancy up to the thirty-seventh week of gestation then rose slightly before delivery. A rise in hemoglobin level occurred from forty-eight hours postpartum to six to eleven months after delivery. Even in women of poor classes the transfer of iron from the mother to the fetus is compensated wholly or to a large extent by dietary iron. In cases where this demand exceeds the retention of dietary iron, the degree of maternal iron deficiency which results is only slight. Where hypochromic anemia in pregnancy is marked, anemia has probably existed before the pregnancy but has been made more apparent by a physiologic hydremia. Therefore, the conception that uncomplicated pregnancy frequently produces a severe degree of hypochromic anemia should be discarded.

The blood loss during parturition varies greatly in degree and often produces severe hypochromic anemia.

F. L. ADAIR AND S. A. PEARL.

Moore, Jocelyn, and Pillman-Williams, E. M.: *Anaemia and Toxaemia of Pregnancy*, Brit. M. J. 2: 528, 1936.

The authors present a clinical and biochemic study of a group of antenatal patients. Some were treated with iron as a routine throughout pregnancy and others not so treated served as controls.

One patient in the iron-treated group of 35 and 6 patients in the control group of 34 showed degrees of toxemia. Only one case had a toxic albuminuria and blood pressure of 160/90.

The toxic cases showed a rise in hemoglobin under iron therapy. The hemoglobin fell in the control cases before toxic symptoms became apparent. In the nontoxic group of patients the hemoglobin varied from a rise of 17 per cent in iron-treated cases and a fall of 8 per cent in the untreated cases. The iron therapy was associated with an improved general well-being and a reduction in the number of colds, etc. No seasonal variation was noted.

Blood urea studies in these groups are reported as well as results of gastric analysis. Sugar tolerance tests on both groups are described. The results were within normal variations in the latter study, except in the postconfinement curve in the toxic group where the fall was more delayed. In the more toxic patients the sugar curves were more markedly raised coincident with the time of the onset of toxemia and in

Donovan, H. C. E.: Heart Disease Complicating Pregnancy, Brit. M. J. 1: 104, 1936.

A report of cardiac cases under observation in the antenatal wards of the Women's Hospital, Sydney, is presented. The incidence of heart cases requiring hospital treatment was 0.255 per cent for the graver cases; those with mild or no symptoms are excluded.

Two maternal deaths occurred. One was due to pulmonary embolism following cesarean section. The other, para xiii, showing advanced myocardial degeneration, died from syncope on the day following an easy short labor. Seventeen patients were delivered by cesarean section; 3 had labor induced; 4 had therapeutic abortion by vaginal route, or abdominal hysterotomy. Labor was shortened in most cases of natural labor by forceps at end of second stage.

Mitral stenosis is the commonest lesion. Myocardial degeneration in elderly multiparas is seen; congenital heart disease, aortic stenosis and aortic regurgitation are less common.

Factors deciding treatment are many, i.e., the character of the lesion, the stage of pregnancy, the previous cardiac and obstetric history, the age and parity and the clinical findings and symptoms, as well as the social and economic position. A full history is most important. All factors must be assessed for the individual case. With complete knowledge of the functional capacity of the heart we still have to estimate the strain of labor upon it. We can estimate this by the previous obstetric history, by pelvic measurements, size of the fetus, its presentation and position. Every labor is an experiment in that the expulsive forces and the capacity of the head to mold are unpredictable. A heart with efficient muscular reserve can stand this experiment safely, but a mistaken estimate can kill or cripple for life a heart that is functionally much below normal. Treatment should not be limited to preservation of the maternal life for health should be maintained.

Indications for terminating labor are discussed. Therapeutic abortion is indicated principally in cases which are getting worse in spite of bed rest and digitalis, and in the more severe forms of aortic disease and congenital lesions. Cesarean section should be performed shortly before term on those in whom auricular fibrillation or decompensation occurred in a previous pregnancy. Trial labor, which saves us from so many errors of treatment in dealing with disproportion, has no place in the treatment of heart disease. The lower uterine segment operation is recommended as reducing the purely operative risks of cesarean section.

F. L. ADAIR AND S. A. PEARL.

Burwell, C. Sidney: The Influence of Pregnancy on the Course of Heart Disease, South. M. J. 29: 1194, 1937.

The manifestations of heart disease may remain essentially unchanged over a period of years with the arrest of the primary causative factor (syphilis, rheumatic fever, thyrotoxicosis), and subsequently certain provocative factors not related to the original disease may supervene, and by supplying an extra burden cause symptoms.

These "precipitating factors" or "removable burdens," which are more or less controllable, include pregnancy, excessive exertion, emotional overstrain, severe anemia, infections, marked obesity.

Pregnancy itself, through the circulatory changes that regularly accompany it, imposes upon the heart a burden of increased work that the author compares to the continuous load of valvular disease rather than to the discontinuous load of physical exertion. This extra work is ordinarily well supported by the heart, but additional burdens may tax it to the extent of exceeding the limits of compensation with resulting congestive failure.

Concerning the pathogenesis of these types of anemia, the author found that they are usually associated with very marked toxic changes of the leucoblastic and erythroblastic tissue of the bone marrow which may lead to a complete exhaustion of hematopoietic function. The character and nature of these anemias can only be determined by a careful study of the morphology of the peripheral blood and of the bone marrow.

The author studied furthermore the clinical picture of 20 eclamptic patients in their eighth to tenth month of gestation and found that in eclampsia the bone marrow is involved to the same extent as other parenchymatous organs due to the general toxic state of the patient. The changes observed in the bone marrow are usually edema and fatty degeneration and these pathologic changes involve predominantly the leucoblastic tissue. These changes are of a toxic nature, probably due to the chemical alteration of the body fluids.

It should be noted, however, that degenerative changes in the bone marrow have been found also toward the end of physiologic pregnancies but in these cases they are only slight.

The author believes that these observations are of considerable importance for the study of the pathogenesis of eclampsia.

Daniachij studied also the bone marrow changes in cases of the nephropathies of pregnancy, preeclampsia, albuminuric retinitis and in hyperemesis gravidarum but the case material was not large enough to permit definite conclusions.

RICHARD E. SOMMA.

Bramwell, Crighton: Treatment of Heart Disease in Pregnancy, Brit. M. J. 1: 1132, 1935.

For the choice of treatment the author divides cardiac cases into three groups and considers treatment for each.

In the more serious cases who are known to have had congestive heart failure in the past and in all those with auricular fibrillation, pregnancy should be prohibited, or if present, and the patients are seen in the early stages, the uterus should be emptied. When seen too late for this, they should be kept under close observation, at rest, and when the heart failure is compensated and the child is viable, a cesarean section should be performed. It is especially important to treat the heart failure primarily.

The second group covers patients whose hearts show signs of failure during the last trimester. Pregnancy should be allowed to pursue its normal course under strict medical supervision and rest. In this group cesarean section is favored by the writer. Opinions differ on this point.

The third group comprises trivial cases in whom pregnancy is allowed to pursue its normal course with the provision of adequate antenatal care and hospitalization for delivery.

Avoidance of physical exertion and ample rest and sleep are stressed for all cardiac cases. One whole day in bed each week is advised as a precaution in some patients during the last two months. Sedatives, tonics and diuretics are mentioned, as well as restriction of salt if edema is present. When bronchitis complicates the picture, it should be treated with rest, inhalations, and a stimulating expectorant. Oxygen therapy is useful. Finally the conviction is expressed that proper medical supervision and hospitalization save many a patient who might develop congestive heart failure.

F. L. ADAIR AND S. A. PEARL.

The author makes a comparison with the total number of deliveries and abortions at the General Lying-In Hospital in Stockholm for the same period (50,014 cases), and the result is as follows: spontaneous deliveries at full term occur less frequently in kyphosis (45 per cent as against 75 per cent in the total material), premature labor occurs more frequently (14 per cent as against 6 per cent), deliveries terminated artificially are more frequent in kyphosis (31 as against 6 per cent) and the mortality among viable fetuses is greater (14 as against 4 per cent). The risk of complications in kyphoscoliosis necessitating an operative delivery is consequently greater and the fetal mortality higher. The author's material is too small to allow an estimation of the death risk of the mothers, but the risk does not appear to be remarkably great. There is always a certain risk of cardiac decompensation, which, however, is not as great as has previously been maintained if the patient is kept under medical control.

In a relatively large number of cases showing slight or moderate contraction of the pelvic outlet, the delivery may proceed spontaneously and without complications even though the fetus is fully developed and of normal size.

Owing to the complications to which kyphoscoliotic women are subjected during pregnancy, labor, and the puerperium, the author emphasizes the importance of their being under medical observation as early as possible. Particular regard should be paid to the heart, to the pelvis, and to the vertebral deformity, which if possible should also be examined by x-ray, above all for the purpose of finding out whether a possible tuberculous spondylitis has been healed in a satisfactory manner considering the increased static strain at delivery.

Induced abortion should be resorted to only in the cases which during the first three months of pregnancy show signs of increasing heart decompensation and in cases of tuberculous spondylitis in which the tuberculosis has not yet healed, or has healed in a way so that the pregnancy brings about a statically weakened condition in the spinal column. During decompensation in the latter half of pregnancy an attempt should be made to get the heart compensated by confinement in bed and stimulation in order later on, when the fetus is fully developed, to end the pregnancy if possible by a cesarean section. In case of decompensation during labor the patient should be delivered as soon as possible. Should the fetal head rest on the floor of the pelvis, forceps is the quickest and to the patient, the most indulgent obstetric instrument. In view of the risk of decompensation after labor the patient should be carefully watched during the puerperium.

J. P. GREENHILL.

Gideon, A.: *Difficulties in Pregnant Women Due to Lying on the Back*, *Acta obst. et gynec. Scandinav.* 15: 295, 1935.

During the latter half of her first pregnancy a patient previously in good health constantly experiences the following symptoms when lying on her back: marked increase in pulse rate, considerable reduction in blood pressure and pulse pressure and retarded breathing. Roentgenologically reduction of heart volume is demonstrable. Subjectively there is a feeling of discomfort and tension in the upper part of the abdomen, difficulty in breathing, etc.

A series of examinations of patients showed that these symptoms appear only when the pregnant uterus rests against the right, posterior part of the peritoneum.

A survey of the effects of pregnancy on the circulatory apparatus shows that a greatly increased disposition toward circulatory disturbances is present during gestation, particularly in the latter half. Evidence is found in the literature that compression of the vena cava inferior, in experiments on animals, causes reduction of blood pressure and increase of the pulse rate.

The author investigated the symptoms commonly present in gravid women in the dorsal position, and also the spontaneous changes in the sleeping position during the

Reduction of mortality from heart disease complicated by pregnancy requires that the obstetrician be informed as early as possible of an underlying cardiac disease and that, having evaluated the heart's functional capacity by observing the patient's reaction to moderate physical exertion, he endeavor to control the known and recognized precipitating factors that may superimpose burdens upon a cardiac mechanism that is already taxed with a double load of pregnancy and preexisting heart disease.

ARNOLD GOLDBERGER.

De Puy, C. A.: Heart Disease Complicating Pregnancy, Calif. & West. Med. 43: 355, 1935.

At the Sinai Hospital in Baltimore, cardiac disease was found to be the second most common cause for obstetric deaths. In no class of patients is prenatal care as important as in this class of patients. On the first signs of any unusual symptoms, such as dyspnea, tachycardia, cyanosis, edema or cough, patients are put to bed and kept under observation. If in a reasonable period of time their symptoms do not subside, their pregnancy must be interrupted. If they reestablish their compensation, they may be permitted up and around again with very limited activities. The aid of an internist, interested in heart disease, is almost a necessary adjunct in the care of these patients.

Having successfully passed through pregnancy to term, the next problem is the management of labor. A few days before labor is due, the patient should be hospitalized and put at complete rest. Labor may be induced or allowed to begin spontaneously. When the pains are well established and the cervix has begun to dilate, the patient is given morphin and this is to be repeated as necessary in the first stage. When the cervix is completely dilated and the head is on the perineum, the patient may be given gas and ether by a competent anesthetist, and the delivery completed by forceps. During the third stage of labor, care should be taken to prevent collapse, as the release of the intraabdominal pressure following the strain of labor is apt to cause serious symptoms. Pituitrin should be given, and a tight binder applied to abdomen. The patient should be allowed to rest in the delivery room for one to two hours before being taken to her room.

Cesarean section is not indicated in this class of cases except when there are complications that would require this method of delivery, for other reasons than the heart lesions.

Following her delivery, the cardiac patient should be kept at rest and not allowed up until she is symptom free. She should not be allowed to nurse her baby, as this puts an extra strain upon her. She must take the required amount of rest and avoid overexertion in the care of her baby. At the first sign of a break in her compensation, she should be put to bed.

J. P. GREENHILL.

Holmgren, B.: Pregnancy and Labor in the Presence of Kyphoscoliosis, Acta. obst. et gynec. Scandinav. 16: 267, 1936.

By way of introduction the author gives an account of 259 cases, previously published, of pregnancies in women having a kyphosis. Of these 33 ($\frac{1}{3}$) died and at least 119 were delivered spontaneously at full term, 11 ($\frac{1}{10}$) of the latter with fatal issue. Large series with no deaths, published by Lindfors and Klafsten show, however, that the death rate of the mother need not be high in cases where an early and careful observation has been made, and the indications have been judiciously considered.

In the author's material, embracing 22 cases of high-grade kyphosis or kyphoscoliosis with 29 observed pregnancies, one death from heart decompensation occurred during pregnancy.

Books Received

OPERATIVE OBSTETRICS. By J. M. Munro Kerr. Emeritus Regius Professor of Midwifery, University of Glasgow, etc. Fourth edition with the assistance of Donald McIntyre, Consulting Obstetric Surgeon, Brashaw Maternity Hospital, etc., and D. Fyfe Anderson, Senior Assistant Professor of Obstetrics and Gynaecology, Glasgow University, etc. With 338 illustrations in the text, 847 pages, William Wood and Company, Baltimore, 1937.

ANNUAL REPORT ON THE RESULTS OF RADIOTHERAPY in Cancer of the Uterine Cervix. First volume: Results obtained in 1930 and previous years. Edited by J. Heyman, M.D., Stockholm. League of Nations Health Organization. Columbia University Press, New York, 1937.

THE BABY'S FIRST TWO YEARS. By Richard M. Smith, Assistant Professor of Pediatrics and Child Hygiene, Harvard Medical School and School of Public Health, etc. With illustrations, 121 pages. New and revised edition. Houghton Mifflin Company, Boston, 1937.

GENITAL ABNORMALITIES, HERMAPHRODITISM AND RELATED ADRENAL DISEASES. By Hugh Hampton Young, Professor of Urology, Johns Hopkins University, etc. With 379 plates, containing 534 drawings by William P. Didusch, 649 pages. Williams and Wilkins Company, Baltimore, 1937.

THE DIARY OF A SURGEON in the year 1751-1752. By John Knyveton, edited by Ernest Gray. 322 pages. D. Appleton-Century Co. New York, 1937.

INSUFFLATION TUBAIRE KYMOGRAPHIQUE par la méthode de Rubin. Par Louis Bonnet, ancien chef de clinique gynécologique à la Faculté de Médecine de Paris. Avec figures, 96 pages. G. Doin & Cie, Paris, 1937.

LEUCOPLASIA DE LA VULVA. Par Dr. Pedro Figueroa Casas, Professor Adjunto de Clinica Ginecológica de la Facultad de Ciencias Médicas de Rosario, etc. Liberia y editorial Ruiz, Rosario, 1937.

PHYSICAL DIAGNOSIS. By Don C. Sutton, Associate Professor of Medicine, Northwestern University School of Medicine, etc. With 298 text illustrations and 8 color plates, 495 pages. The C. V. Mosby Company, St. Louis, 1937.

TEXTBOOK OF DIAGNOSTIC ROENTGENOLOGY. By Lewis J. Friedmann, M.D., Director of Roentgen Ray Department, Bellevue Hospital, etc. With 638 illustrations, 622 pages. D. Appleton-Century Co., Inc., New York, 1937.

MALADIES DES FEMMES ENCEINTES. Tome III. Affections de la Peau. Par Henri Vignes, avec la collaboration de F. Hanoun et G. Vial. 202 pages. Masson & Cie, éditeurs, Paris, 1937.

SYNOPSIS OF ANO-RECTAL DISEASES. By Louis J. Hirschmann, Professor of Proctology, Wayne University, etc. With 174 text illustrations and 6 color plates, 288 pages. The C. V. Mosby Co., St. Louis, 1937.

PRENATAL AND POSTNATAL MANAGEMENT. By J. St. George Wilson, Hon. Obstetric and Gynaecological Surgeon, Royal Infirmary, Liverpool, etc. With a foreword by Sir Comyns Berkeley. With 80 figures and a color plate, 206 pages. William Wood & Co., Baltimore, 1937.

PROPEDEUTICA OBSTETRICA. Prof. Arnaldo de Moraes, Professor Cathedrico de Clinica Gynecologica da Faculdade Nacional de Medicina da Universidade do Brasil. 5. Edicao. Com 490 paginas e 158 gravuras. Grafica Suer, Rio de Janeiro, 1937.

THE THERAPEUTIC PROBLEM IN BOWEL OBSTRUCTIONS. By Owen H. Wangenstein, M.D., Ph.D., Professor of Surgery, University of Minnesota, etc. Ninety illustrations, 360 pages. Charles C. Thomas, Springfield, Ill., 1937.

latter half of pregnancy. Among 653 gravid women, 197 (30 per cent) experienced different symptoms when lying on the back during the latter half of pregnancy (tenderness, fatigue, pains in the abdomen or back, stronger movements of the fetus, palpitation, etc.); forty-two patients (6.4 per cent) could not lie on the back at all. In more than one-third of the patients the sleeping position was changed in the latter part of pregnancy.

The author draws the conclusion that the common symptoms experienced by pregnant women when reclining on the back probably are caused by more or less complete compression of the vena cava by the pregnant uterus, possibly in connection with upward pressure on the diaphragm.

J. P. GREENHILL.

Pohl, Armin: *Thyroid and Pregnancy*, Arch. f. Gynäk. 160: 447, 1936.

There is a definite and marked increase in size and function of the thyroid during pregnancy. This change is shown by the increase in the minute blood volume of the heart. The typical thyroid of pregnancy can be produced by very small quantities of the thyreotropic hormone of the pituitary. Large doses of pregnancy serum produce definite changes in the thyroid in animal experiments. The author found no evidence of the development of toxic symptoms during pregnancy. A pre-existing Basedow disease becomes worse in only 50 per cent of instances and results fatally in only 6.4 per cent. Some authors claim that the toxic condition is improved by pregnancy.

This increase in thyroid function during pregnancy is not pathologic but is a true work hypertrophy. The other glands are not changed by this action of the thyroid in pregnancy; on the other hand, this change is independent of the function of the other glands of internal secretion.

RALPH A. REIS.

Item

American Board of Obstetrics and Gynecology

The general oral, clinical and pathological examinations for all candidates (Groups A and B) will be conducted by the entire Board, meeting in San Francisco, California, on June 13 and 14, 1938, immediately prior to the meeting of the American Medical Association.

Application for admission to the June, 1938 Group A examinations must be on an official application form and filed in the Secretary's Office before April 1, 1938.

The annual informal Dinner and General Meeting of the Board will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association will be the guest speaker, and the Diplomates certified at the preceding days' examinations will be introduced individually. All Diplomates are invited to attend the dinner meeting, and to bring as guests their wives and any persons interested in the work of the Board.

For further information and application blanks address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pa.

So let us be grateful to Joseph Price for his uncompromising advocacy of what he believed to be right as well as for his brilliant professional attainments, for both played a part in laying the foundations of modern pelvic surgery.

The problem of endometriosis is one of the most important in gynecology and well worthy of a place among the subjects dealt with by your Joseph Price Orators. Tonight, I propose to deal with the problem as a pathologic and clinical entity, and if I traverse well worn and familiar ground you will understand that this is unavoidable if the picture which I am going to paint is to be a complete one.

Endometriosis may be defined as the growth of endometrium in an abnormal situation, and it is said to be direct or internal when the endometrium lining the uterine cavity invades the subjacent muscle, indirect or external when the endometrial tissue reaches its destination by some other route.

The physiologic activity of the misplaced endometrium may produce an accumulation of the secretions poured out during menstruation or an irritative hypertrophy of the tissue invaded, the result in either case being a gross and frequently destructive lesion of the pelvic organs. In this way arise the adenomyomata, endometriomyomata, endometriomata and hematomata of different authors, but as a simple terminology is conducive to clear thinking and as the lesions are due solely to the activity of misplaced endometrium, I am of opinion that the terms internal and external endometriosis are sufficiently comprehensive for all purposes and that the others should be discarded as superfluous and needlessly confusing.

Further, as the term external endometriosis does not imply that the source of the misplaced endometrium is necessarily the uterine cavity, its use in the way suggested need not offend the susceptibilities of those who hold other views on etiology.

THE PATHOLOGIC PROBLEM

The evolution of our knowledge of endometriosis is one of the most fascinating chapters of gynecologic pathology and will be associated for all time with the names of two American workers, Thomas S. Cullen and John A. Sampson.

Uterine tumors containing both smooth muscle and glandular elements were recognized and described more than fifty years ago, but they aroused very little interest until the appearance of von Recklinghausen's important monograph on adenomyomata in 1896.¹ Up to that time the glandular elements were believed to be of Müllerian origin, but von Recklinghausen put forward the view that in the great majority of cases they were derived from the Wolffian body, although occasionally they might come direct from the uterine mucous membrane. The Wolffian

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THE PROBLEM OF ENDOMETRIOSIS*

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(Professor of Obstetrics and Gynecology in the University of Manchester)

I DEEPLY appreciate the honor of being invited to deliver this oration in memory of one of the great pioneers of abdominal and pelvic surgery.

Joseph Price was a disciple of that turbulent Scottish genius, Lawson Tait, and himself possessed so many of the qualities which distinguished that famous man that there is ample justification for describing him as Tait's American counterpart.

Both men were clinicians of outstanding ability who based their methods on accurate pathology, both were superb craftsmen whose achievements in the practical field of surgery were equaled by few and surpassed by none of their contemporaries.

I must add that both were keen fighters who thrived on controversy and who gave and expected no quarter in dealing with their adversaries.

Autre temps, autre mœurs; we now live in an age of compromise and heated discussions have almost become a thing of the past, but, although more pleasant, this method of settling our differences is not always the best and in Price's day, when great principles were at stake, might have seriously interfered with surgical progress.

*The Joseph Price Oration. Presented at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20 to 22, 1937.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

At a meeting of the Gynaecological Society of the Netherlands in May, 1904, Semmelink and Joselin de Jong⁹ showed a specimen of extensive endometriosis of the pelvic organs in which both ovaries were cystic and one contained endometrial tissue in the hilum with a process extending into the stroma.

Finally, in 1920, Cullen¹⁰ published a paper on the distribution of adenomyomata, containing uterine mucosa, and described three specimens of ovaries which he had obtained from different sources and in which endometrium was present.

While undoubtedly of great interest and importance, these specimens were looked upon as pathologic curiosities until the appearance of Sampson's classical paper on perforating hemorrhagic cysts of the ovary in the summer of 1921.¹¹ This author called attention to a type of hemorrhagic ovarian cyst or ovarian hematoma which was important not only because of its frequency but also because of the nature of the adhesions resulting from the escape of its contents into the peritoneal cavity. Sampson believed that the leakage was due to a perforation which later became sealed by adhesion to neighboring structures.

In 1910 his attention had been first directed to the dense peritoneal adhesions which may result from the escape of the cyst contents and in 1912 he had observed their association with adenomyomata of the posterior uterine wall and adhesions between the latter and the rectum, but in the paper quoted he was able to bring forward histologic evidence that tissue of endometrial type was invariably present in the ovary, particularly in the neighborhood of the perforation.

Sampson concluded that here was a primary growth of the ovary containing tissue resembling endometrium both anatomically and physiologically and by leakage of the cyst contents capable of extension to the neighboring structures in a manner similar to that found in the case of rupture of a papilliferous or malignant ovarian tumor.

In his 1921 paper Sampson offered no explanation of the frequency with which endometrial tissue is found in the ovary, but in a subsequent communication in 1922,¹² he propounded his theory of retrograde menstruation and cellular spill. During menstruation, some of the menstrual blood with its normal content of endometrial fragments may pass backwards through the Fallopian tubes and reach the pelvic peritoneal cavity. Arrived there, the fragments implant themselves on the serous surface either because of their inherent powers of growth or because the peritoneum has been damaged by the irritant action of the menstrual blood. The majority of the fragments attach themselves to the pelvic organs and anterior and posterior cul-de-sac, but the movements of bowel and bladder make a much wider dissemination possible and readily explain the occurrence of endometrial tissue in situations as far removed from the pelvis as the umbilicus.

That retrograde menstruation and cellular spill do occur is within the experience of every abdominal surgeon who at some time or other must have seen blood dripping from the abdominal ostia or the serous surfaces of the pelvis splashed with purplish endometrial implants.

I am a wholehearted believer in Sampson's theory and consider that it is applicable to practically all cases of external endometriosis.

Many gynecologists find it difficult to reconcile the occurrence of umbilical and inguinal endometriosis with a belief in Sampson's theory, but surely this is not difficult if it is remembered that hernial protrusions of the peritoneum are frequently found in these situations.

theory gained wide support but, even before its appearance, Cullen had entered the field and was laying emphasis on the mucosal origin of these tumors. In 1903² he reviewed the literature and reported 22 cases which he had examined up to that time and five years later³ he published a comprehensive monograph on the subject and brought forward the most conclusive evidence that uterine adenomyomata were generally of mucosal origin.

Cullen's theory carried the day as far as the diffuse uterine tumors were concerned, and he himself was satisfied that it also offered an adequate explanation of the origin of subperitoneal and intraligamentary growths. In 1914⁴ he went a step further and expressed the view that the glands in adenomyomata of the rectovaginal space undoubtedly arose from uterine mucosa or from remnants of the Müllerian duct.

There still remained a number of extrauterine tumors, notably those found in the round ligament, ovary, and umbilicus, whose origin was less easy to explain.

In 1898⁵ Iwanoff described a case of adenomyoma complicated by carcinoma and sarcoma and concluded that certain cystic spaces in the tumor were of serosal origin.

This was an observation of the first magnitude and offered an explanation of the origin of these tumors which was capable of almost limitless application. The serosal theory found many adherents and Robert Meyer⁶ gave it his blessing and elaborated from it his own theory of epithelial heterotopy or displacement. Meyer pointed out that this infiltrative activity of the epithelium was in no sense malignant but was part of a healing process associated with a pre-existing inflammation and not limited to any one part of the body. While the mucosal theory was adequate for the great majority of uterine tumors, he thought that heterotopy of serosal epithelium was the probable explanation of the existence of the epithelial spaces and cysts in most of the extrauterine swellings found between the rectum and the genital tract.

The stage was now set for the appearance of Sampson and even those who do not agree with all his conclusions must admit that his brilliant contributions from 1921 onwards have floodlit the controversial scene and enabled us to view the whole problem of endometriosis, both uterine and extrauterine, in proper perspective.

As long ago as 1899 Russell⁷ described a case in which uterine mucosa was present in the ovary and which he thought originated from aberrant portions of the Müllerian duct.

About the same time Pick⁸ found cysts of the ovary containing syrupy, chocolate-colored or reddish brown bloody contents and lined by a mucous membrane made up of elements similar to those found in the uterine mucosa, and he suggested the term *adenoma endometrioides ovarii* for such endometrial invasions of the ovary.

eclipse during the ascendancy of von Recklinghausen's Wolffian theory. They were revived, however, by von Franqué¹⁹ in 1900 and from that time onwards the theories of inflammatory causation and mucosal origin became complementary and inseparable.

The inflammatory theory was also linked up with the serosal theory, and as already stated Robert Meyer made it an essential part of his phenomenon of epithelial heterotopy, whether applied to the uterine mucous membrane or to the peritoneum.

In the case of the uterine mucosal growths, Meyer also hinted at the possibility of a mechanical factor when he wrote that, if a mechanical lesion were present such as might be caused by therapeutic means or by gestation or parturition, neither a small muscular interstice open on the mucous aspect nor the interfascicular connective tissue would be capable of offering resistance to the ingrowth of epithelium.

If Sampson's theory be correct, a mechanical factor would certainly appear to be of importance in external endometriosis, as backward displacement of the uterus or distortion of its cavity may favor regurgitation of menstrual blood and certain diagnostic and operative procedures actually propel some of the uterine contents into the peritoneal cavity.

The uterine endometrium differs from all other mucous membranes in that it passes through the different phases of the menstrual cycle, and as true endometriosis is never observed unless physiologically active endometrial tissue is present, it is reasonable to deduce that the causal factor must be closely related to those which control menstruation.

In a more recent communication Meyer²⁰ has ascribed uterine endometriosis to basal glandular hyperplasia, his view being that the basal layer of the endometrium, the matrix for the regeneration of the mucous membrane after the more superficial layers have been cast off during menstruation, frequently becomes hyperplastic in response to the monthly calls made upon it, and in certain cases, may exceed its physiologic limits and invade the uterine wall. He believes that the invasive powers rest in the peculiar cellular stroma which is able to exercise a histolytic action on the structures penetrated in a manner which foreshadows malignancy in a mild way.

Other observers, however, believe that the basal layer undergoes little change during the menstrual cycle and if this be so one might reasonably look upon it as an inert barrier lying between the actively proliferating layer and the subjacent muscle. Such a barrier might become less efficient or cease to exist as a result of injury, inflammation or an excess of the normal hormonal stimulus.

In the paper already quoted Robinson expresses the view that the cause of endometriosis is an excess of ovarian hormones which under certain biologic conditions stimulate the dormant celomic rests to adenoid formation. The latter also respond in a functional way as expressed clinically by menorrhagias and metrorrhagias, by the forma-

In my own practice I have had one example of inguinal and one of umbilical endometriosis and in both instances there was extensive endometriosis of the pelvic cavity. Further, the patient with the umbilical lesion had at one time worn a truss for umbilical hernia.

Sampson's views have been widely but not generally accepted, and it is somewhat ironical that his accurate description and logical interpretation of pelvic endometriosis have led to a revival of the serosal theory in opposition to the one which he himself has brought forward.

Robinson¹³ has pointed out that the celomic epithelium is the structural source of the generative organs, and he explains the evolution of external endometriosis as a topical awakening of the genetic potentialities in some of the celomic rests. Novak expresses similar views.

The serosal theory has therefore been amplified and has now become the celomic theory but, in spite of its infinite possibilities, I still prefer the one propounded by Sampson as I believe that it offers a more reasonable explanation of the "splashing" of the serous surfaces found in external endometriosis.

Admittedly there are a few pathologic curiosities, such as the brachial endometriosis described by Navratil and Kramer,¹⁴ which neither theory is able to explain satisfactorily but which may conceivably arise as a result of metastatic or embolic endometriosis, either by the lymphatics as suggested by Sampson in 1922¹⁵ and two years later by Halban¹⁶ or by the veins as actually demonstrated by Sampson in 1927.¹⁷

Having discussed the possible sources of the misplaced endometrium, the factors which favor endometriosis must next be considered.

The most extreme example of endometrial invasion is seen in carcinoma of the body of the uterus. Here the affected mucous membrane proliferates and forms a tumor which may fill the uterine cavity. Fragments may be broken off and implant themselves on the mucous surfaces of the lower genital tract or be carried along the Fallopian tubes and reach the peritoneal cavity. The malignant endometrium may also penetrate and destroy the deeper structures in the uterine wall, and some of the cells may enter lymphatics and blood vessels and be transported to distal organs. Here the invasive powers rest in the altered character of the malignant cell but in the case of endometriosis, in which the sequence of events is similar, there must be some other factor which induces normal endometrium to break its bounds without disturbing its functional activity.

In 1887 Chiari¹⁸ published his observations on salpingitis isthmica nodosa and concluded that the tubal and cornual nodes characteristic of that condition and indistinguishable from adenomyoma were the outcome of a chronic salpingitis. His views were immediately confirmed by other workers but suffered a temporary

and possible reasons for this may be its sheltered position when the uterus is retroverted, the proximity of the fimbriated end of the Fallopian tube, the absence of a serous covering, the monthly breech of surface continuity associated with ovulation, and the (possibly) greater concentration of estrin in that organ.

Endometriosis of the ovary results in the formation of the well-known perforating hemorrhagic cyst described by Sampson and now recognized as one of the most important lesions with which the pelvic surgeon has to deal. In the early stages the affected ovary is adherent and on separating it a small quantity of black, treacle-like material escapes. Its surface appearance is not much altered except for some dilated vessels which run in parallel lines across the hilum, but on bisection it will be found that a considerable amount of the interior has been excavated by the invading and secreting endometrium. One might compare the ovary at this stage with an apple which has become rotten at the core, although apparently quite sound externally.

Later the ovary becomes distended with the products of endometrial activity and forms a considerable tumor adherent to the posterior surface of the uterus and other adjacent structures.

In early cases the misplaced endometrial elements are readily demonstrated, but when the entire ovary has been converted into a cyst this becomes more difficult. The naked eye appearances of such cases are quite unmistakable, however, and provide sufficient evidence on which to base a diagnosis of endometriosis.

Next in importance is the pouch of Douglas and the preference shown for this site is probably due to the fact that endometrial fragments gravitate there and are then less likely to be disturbed by intestinal movements.

The most characteristic feature of endometriosis in this situation is the tucking up of the rectal wall to the back of the uterus. Nodules are also palpable in the affected area, and there may be considerable thickening of the uterine and rectal walls.

Implants are also frequently observed in the uterovesical pouch, but they rarely give rise to lesions of clinical importance.

External endometriosis of the uterus is an almost invariable accompaniment of ovarian and rectovaginal endometriosis and in exceptional cases may be the most important lesion. It varies in degree from a mere roughening of the surface to which adjacent structures have been adherent to a palpable tumor closely resembling a fibroid and liable to be mistaken for it unless carefully examined.

External endometriosis may also involve other structures either adjacent to those already mentioned or more distant but as they are all variations of the same theme they need not be described separately.

In my own series of 241 cases of external endometriosis, one or both ovaries were involved in 103, the rectovaginal space in 62, and the

tion of tarry cysts in the ovary, and by the periodic enlargement and shrinkage of the adenomata at the beginning and at the end of the menstrual period.

The follicular hormone is responsible for the proliferative phase of the menstrual cycle and when secreted in excessive amounts as in metropathia hemorrhagica produces an exaggeration of the hypertrophic changes characteristic of this phase and also some degree of endometriosis. With these facts in mind Jeffcoate and Potter²¹ examined the clinical and pathologic material from 111 cases of pelvic endometriosis and in the great majority were able to find evidence of follicular overactivity.

They concluded that endometriosis is analogous to hyperplasia and is produced by excessive production of estrin irrespective of the primary source of the endometrial elements.

In summing up the question of etiology, I would say that in the majority of cases the theories of Cullen and Sampson adequately explain the source of origin of the endometrial elements, that trauma and inflammation may be predisposing factors but that the exciting cause of the invasive process is probably to be found in an excessive secretion of the hormone responsible for endometrial proliferation.

The naked eye and microscopic appearances of endometriosis are unmistakable.

In the case of the uterus, whether the endometriosis be internal or external, there is a diffuse or nodular thickening of the muscle wall composed of hyperplastic fibromuscular tissue and seams or islets of endometrium. The presence of the latter distinguishes the tumor from a fibromyoma as also does the absence of a capsule.

The two most important varieties of internal endometriosis are the diffuse lesion in which one wall of the uterus is affected and the organ uniformly enlarged, and the cornual in which the fundus is lopsided or saddle-shaped.

My cases of internal endometriosis include nine diffuse and twelve cornual lesions, but there were probably others which escaped recognition.

In external endometriosis the earliest manifestation is the presence of a number of minute purplish blood cysts or implants on the surface of the pelvic organs and in the anterior and posterior cul-de-sac.

The subsequent life history of these implants depends first of all on their proliferative activity and second on their situation. The ovary and pouch of Douglas are the most favorable sites for continued growth and the majority of lesions of clinical importance are to be found in these situations. Sampson early recognized the frequency and importance of ovarian endometriosis and regarded the ovary as a sort of incubator or hotbed. There is no doubt that conditions in the ovary are peculiarly favorable for the further development of the implants

Minor degrees of both internal and external endometriosis are no doubt extremely common but unless the patients complain of symptoms which require surgical treatment the condition is not likely to be recognized at this early stage.

From an examination of his pathologic material O. Frankl²⁴ is of the opinion that internal endometriosis is met with about one-twelfth as frequently as uterine fibroids. In the pathologic department of St. Mary's Hospital, Manchester, during the ten years 1926 to 1935, the relative frequency of the two conditions was as one to seventeen, there being 137 specimens of internal endometriosis and 2,358 of fibroids.

Thanks mainly to Sampson's work it is now recognized that external endometriosis occurs much more frequently than the internal variety.

In the St. Mary's Hospital series just referred to, the external endometriosis-fibroid ratio was one to six. The figures for my own cases over a period of ten years give a ratio of one to four and this is probably a more accurate estimate, as pathologic specimens are not always available when the rectovaginal space alone is involved.

Sampson called attention to the frequency with which pathologic lesions arising from endometriosis of the pelvic peritoneal cavity are encountered during abdominal operations and stated that he had found them 37 times in 170 abdominal operations performed for pelvic conditions between thirty and fifty years of age.

Excluding minor degrees of no clinical importance, I have met with 241 cases of external endometriosis in eleven and a half years, a figure which represents about 10 per cent of all abdominal operations performed by me during that period.

To sum up, it may be said that for every 100 cases of uterine fibroids there are 6 cases of internal and 25 cases of external endometriosis and that the latter is met with as the principal lesion or as an important complication in not less than 10 per cent of all abdominal operations on the female genital organs.

To determine the influence of endometriosis on the patient's general health, it is necessary to consider the frequency and severity of the principal symptoms, abdominal pain, menorrhagia, dysmenorrhea, and dyspareunia.

Pain in the lower abdomen is an important symptom of endometriosis, both internal and external, and may be the chief symptom of complaint.

Recently, I saw a patient who was prostrated by recurring attacks of acute abdominal pain, having no relation to the menstrual period. Radiologic investigation of the alimentary and urinary tracts had already been carried out but the results were negative. On examining her pelvic organs bimanually, I was able to make out some asymmetry of the uterine fundus and therefore decided to explore the abdomen.

The lesion was found to be an endometriosis of both uterine cornua and removal of the uterus resulted in a complete cure.

ovaries and rectovaginal space in 71. In the remaining five cases the lesions were in other situations. The ovaries were therefore affected in over 70 per cent of all cases.

I have met with the following unusual examples of endometriosis:

a. Both ovaries, pelvic colon and appendix, the last named being adherent close to the right ovary.

b. Ovary and laparotomy scar, operation for acute appendicitis fifteen years previously.

c. Left ovary and uterine cornua, the right ovary and both Fallopian tubes removed ten years previously for pyosalpinx and tuboovarian abscess.

d. Ovary, rectovaginal space and small intestine, the last almost obstructed in several places.

e. Ovaries, uterus, bladder, and inguinal canal, the ureters obstructed and dilated.

f. Ovaries, uterus, rectovaginal space and umbilicus.

Pelvic infection and newgrowths of the uterus and ovaries, either benign or malignant, may be complicated by endometriosis, but with the exception of uterine fibroids their association is too rare to be anything but accidental.

With fibroids it is quite otherwise and I found these tumors present in more than one-third of the cases of external endometriosis. This fact may be interpreted in three ways: the fibroids may represent the irritative reaction to a preceding endometriosis as suggested by Sampson, both fibroids and endometriosis may be produced by the same hormonal stimulus, a view put forward by Jeffcoate, or the presence of fibroids may predispose to retrograde menstruation and endometriosis by displacing the uterus and distorting its cavity.

As regards more remote sequelae, Sampson has observed malignant tumors of the ovaries and peritoneum which appear to have originated in benign endometrial implants²² and more recently Frankel and Schenk²³ have suggested that all ectopic pregnancies are due to implantation of the zygote on misplaced endometrial tissue.

THE CLINICAL PROBLEM

The importance of the clinical problem rests on the fact that every woman is exposed to the danger of endometriosis during the reproductive period of her life and that the lesions which may result are of a diffuse or infiltrative character and except in their early stages not readily amenable to conservative treatment.

Further, endometriosis seriously interferes with the conservative treatment of other conditions such as uterine fibroids with which it is so frequently associated.

To appreciate the extent of the problem, it is necessary first of all to obtain some idea of the incidence of endometriosis and then to assess the damage which it may inflict on the patient's general health and reproductive function.

have very little experience of radiologic treatment and prefer to remove the uterus, preferably by total hysterectomy together with both appendages. It is unnecessary and, in fact, dangerous to dissect out growths from the bowel wall, as these will retrogress after the ovaries have been removed.

One of my patients had chronic intestinal obstruction from the presence of two endometriotic lesions in the ileum, but the obstruction completely disappeared after the uterus and appendages had been removed. Alfred Gough²⁶ has also reported a case in which acute intestinal obstruction was produced by a lesion involving the rectal wall. The uterus and appendages were removed and a temporary colostomy performed, but it was possible to close the latter within a short time and the patient has now completely recovered.

In less severe cases and particularly in younger women, treatment should, if possible, be conservative, but it must be realized that this may only relieve the symptoms for a time and have to be followed at a later date by a more radical operation.

As far as I know only two of my patients have become pregnant after conservative treatment, and a considerable number have not obtained complete relief.

The abdominal operations performed in my own series were as follows:

Total hysterectomy with both appendages	107
Subtotal hysterectomy with both appendages	98
Total hysterectomy with one appendage	6
Subtotal hysterectomy with one appendage	17
Subtotal hysterectomy, appendages not removed	6
One appendage removed	14
Other conservative operations (excision of nodules, etc.)	14
Total	262

There were three deaths, one from peritonitis and two from embolism, an operative mortality of a little over 1 per cent.

Some ovarian tissue was left behind in 21 per cent of the cases, but true conservative treatment, that is to say treatment which does not interfere with subsequent pregnancy, was possible in only 10 per cent. If patients over thirty-five years of age are excluded, however, this percentage is 30 in 83 cases.

The average person's reaction to these figures will probably be one of surprise that so many radical operations were considered necessary, but it must be remembered that to be successful, conservative treatment should not only conserve function but also cure the disease. Many keen advocates of conservative surgery are likely to forget this in their anxiety to preserve the reproductive organs.

I must confess, however, that the radical nature of the surgical treatment of endometriosis depresses me when it becomes necessary

Menorrhagia or epimenorrhagia is complained of in about 40 per cent of the cases and may be extremely severe, especially if the uterus is involved. That the excessive loss is not due to associated fibroids is shown by the fact that the incidence of fibroids in those patients who complained of this symptom is very little higher than that for the whole series.

Dysmenorrhea, particularly if of recent origin is undoubtedly the most characteristic symptom of endometriosis but is only present in rather less than half of the cases. Frequently, it is of great intensity and becoming progressively worse. The pain may be referred to the hypogastric or sacral regions or to one iliac fossa. In the latter event the corresponding ovary is usually involved but occasionally the lesion is situated in the uterine cornu of that side.

Miles Phillips²⁵ has described a series of these cases and my own observations confirm his view that a cornual endometriosis is a rare but important cause of unilateral pain at the menstrual periods.

Dyspareunia may be an extremely troublesome symptom and cause the patient much pain and mental distress. It is met with in its most severe form when the endometriosis involves the structures behind the posterior vaginal fornix.

Other symptoms, less frequently complained of, are "shooting" or "electric" pains in the vagina, pain in one or other leg, difficult or painful defecation, and constipation sometimes amounting to chronic or even acute intestinal obstruction.

I have met with severe degrees of pelvic endometriosis which were almost painless but this is exceptional; on the other hand the pain is frequently so severe that the patient is willing to undergo any treatment, however, radical, in order to obtain some relief.

The next point for consideration is the influence of endometriosis on fertility, and in this connection it is important to consider the age incidence of the disease. In my own series of cases, 88 per cent were operated upon between the ages of thirty and fifty, 28 per cent under thirty-five and 10 per cent under thirty. Twenty per cent of the patients were single.

Excluding cases in which there were associated uterine fibroids, single women, and women who had been married less than three years, 40 per cent of the remainder were sterile, 32 per cent had not been pregnant for at least ten years and 23 per cent for at least five years.

These figures prove that endometriosis has a serious adverse influence on fertility. No doubt ovarian dysfunction is partly responsible for this, but I think the main cause is the severe and infiltrative character of the lesions produced by the misplaced endometrium.

I now come to the treatment of endometriosis. When the lesions are extensive, this must be radical and either surgical or radiologic. I

social point of view. For the proper appreciation of this fact we are mainly indebted to the brilliant researches and painstaking observations of John A. Sampson, and on this, my first visit to the United States, I would like to give expression to the respect and admiration which I feel for his work and which I know are shared by every British gynecologist.

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IMPROVEMENTS IN THE OPERATIVE TREATMENT OF CARCINOMA OF THE LARGE BOWEL*

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THE general principles underlying the operative treatment of carcinoma of the large bowel are not new. The perineal approach used in the primitive operations of Faget in 1739, Lisfranc in 1826, and in the improvements of Cripps and Allingham and others, was continued in the more radical method of Kraske of 1885. The inadequacies of the Kraske operation led to the preliminary colostomy of Schede in 1887, then to the deliberate combined abdominoperineal resection with perineal anus of Maunsell in 1892 and finally to the combined operation with abdominal colostomy of Quéno in 1896. Since this time the many operations for cancer of the rectum and rectosigmoid which have appeared over the names of various surgeons have been largely modifications or repetitions of work previously done.

Likewise the principles underlying resection of the colon with exteriorization are old, having been devised by Bloch in 1892 and especially by Paul in 1895. Mikulicz popularized the procedure, and while

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in women under thirty-five years of age, but the only solution is either to prevent the occurrence of endometriosis or to diagnose the lesions at an earlier stage of their development.

If endometriosis be the result of ovarian dysfunction, it may be possible to recognize the latter by its effect on the menstrual cycle, and when clinical endocrinology has advanced to the stage when the specific hormones can be used with precision, to successfully treat it.

In the meantime it should be possible to reduce the incidence of external endometriosis by treating conditions such as subinvolution, backward displacements of the uterus, and uterine fibroids, which may predispose to retrograde menstruation, and by carrying out the various intrauterine diagnostic and operative procedures at a time and in a manner least likely to drive fragments of endometrium into and through the Fallopian tubes.

The present-day custom of advising girls to lead a normal and active life during the menstrual period is open to objection for the same reasons, and it is quite possible that some of the pelvic endometriosis met with today is due to woman's emancipation and her determination to ignore or minimize the handicap of the menstrual function.

The other alternative is to operate on cases at a stage when it is possible to excise or destroy early lesions in the ovary or elsewhere. Small implants can be cauterized, nodules in the rectovaginal space dissected out or the affected part of the ovary resected. I have read of so-called tarry cysts being shelled out from the ovary, but I doubt if this is ever possible, as a true endometriosis eats away the substance of the ovary and cannot be enucleated.

Conservative treatment of this kind is only possible if a correct diagnosis is made early in the course of the disease, and this necessitates a proper appreciation of the importance of such symptoms as acquired or increasing dysmenorrhea, particularly if associated with menstrual irregularity, pain in the vagina or on defecation, and high dyspareunia.

Recognition of the characteristic physical signs is equally important, and the earliest of these is either some diminished mobility or some asymmetry of the uterus. The presence of a nodular swelling behind the cervix is usually conclusive evidence of endometriosis in that situation, but occasionally small fibroids adherent in the pouch of Douglas may confuse the diagnosis.

Dysmenorrhea or dyspareunia of recent origin should always arouse a suspicion of endometriosis, and in the absence of well-marked physical signs be sufficient to warrant a careful examination under anesthesia or even an exploratory abdominal operation.

I have dealt with the problem of endometriosis in its pathologic and clinical aspects and have endeavored to stress its importance from the

the large intestine. For growths of the rectum and rectosigmoid, we usually employ a one-stage combined proctosigmoidectomy. Through a left rectus incision, under spinal anesthesia, the sigmoid and rectum with adjacent peritoneum and tributary lymph glands are liberated to the floor of the pelvis and the superior hemorrhoidal and inferior mesenteric vessels are divided, between double ligatures. In no way is the very radical nature of the operation compromised. The lower level of viability of the sigmoid having been determined by color and arterial pulsation, a long folded gauze tape is tied about the bowel at this point. If necessary, restraining peritoneal attachments to the descending colon are sufficiently divided that viable sigmoid may be brought to the perineum. No attempt is made to form a pelvic diaphragm or to peritonize denuded surfaces, experience having shown such procedures to be unnecessary. The tape having been packed against the pelvic floor, the abdominal incision is closed. Through a median postanal incision the tape and the attached loop of bowel are withdrawn. Dressings are applied, the cancerous loop then amputated and a rectal tube tied into the end of the sigmoid. A week later the two partitions between the terminal sigmoid and anus are divided and the mucous edges united with fine wire sutures so that a single opening is formed. If the pelvic floor or anus has been invaded by the cancer it is widely excised and removed attached to the rectum and segment of sigmoid.

A second method adapted to anterior rectal growths which are adherent to or have invaded the prostate is, after completing the abdominal portion of the operation, to turn back a flap from the anterior perineum similar to that used by Young for prostatectomy, and deliver and excise the diseased loop of bowel. The proximal end of the sigmoid is then brought out through the split anus, after which the perineal wound is closed. Despite these extensive operations the patient may not infrequently be permitted out of bed by the tenth day, and to go home with a small superficial granulating wound area by the fourteenth day.

If when the tissues about the cancer are reached, they are found to be indurated and adherent, one may suspect a perirectal infection. The abdominal part of the operation should then be terminated and the liberation of infiltrated tissue completed from below to reduce the danger of peritoneal contamination.

Oblique muscle splitting incisions we have found of great advantage in the excision of the cecum, ascending colon, hepatic and splenic flexure, and the descending colon. As a rule the incision follows the line of one of the lower intercostal nerves, splits the external oblique and in part the transversalis muscle, divides the anterior and above the linea semilunaris, the posterior sheath of the rectus abdominis which muscle is usually retracted or may with the internal oblique

he did not claim priority his name has remained attached to the method since his paper of 1902. Upon the broad foundations laid by these and other surgeons there is still much room for technical improvements.

Perineal colostomy long in disfavor with surgeons but invariably requested by the patient is advantageous if properly performed. The widely used Kraske operation left such a train of stenotic and cicatricial anal openings through which, to the disgust of all concerned, the overflow from a distended colon dribbled almost constantly, that the perineal opening acquired undeserved opprobrium. As the great mitigating factor in enabling one to endure an abdominal colostomy is the adequate emptying of the colon at fairly regular and infrequent intervals, it seems logical that this should apply also to the perineal opening. But the perineal opening commonly became strictured because the bowel of which it had been formed was avascular and had sloughed away. Clearly it is very important to bring viable bowel to the perineum. But this may require not only ligation and division of the superior hemorrhoidal and inferior mesenteric vessels but in certain cases the partial mobilization of the descending colon by dividing its peritoneal attachments, in order to free 12 to 15 cm. of living bowel to reach from the pelvic brim to and through the pelvic floor. Obviously such mobilization cannot be carried out through the perineum and in any case the surgeon should determine the line of demarcation between vascular and avascular bowel by the transition from pink to leaden color and from pulsating to nonpulsating vessels. Many surgeons have devised methods to constrict or obstruct the artificial anal opening not appreciating the advantages of an open orifice. If the perineal anus is large and open, then about three months after operation, a more regular evacuation is established. There is more complete and less frequent emptying of the colon and usually a five- to ten-minute warning of the approaching defecation develops. Some of the patients find that a saline enema every two or three days gives them an interim of almost complete freedom, others that a small amount of a sodium or magnesium sulphate or similar laxative (not mineral oil) taken in cold water on arising will immediately after breakfast so empty the colon that they may then go twenty-four to seventy-two hours without evacuation, when the procedure must be repeated. Most of the patients avoid the more laxative foods and wear a rather small pad and T-bandage, others find a minute plug of cotton adequate. A few despite the loss of sphincters eventually find it unnecessary to wear any protection over the opening. Rarely is a secondary operation for better control requested.

As the perineal opening made with viable bowel is convenient and greatly preferred by the patient, we have not for seven years used a permanent abdominal colostomy in any case of removable cancer of

and suture of the bowel edges also with fine wire sutures at the time of, or six to ten days after, the division of the spur. To avoid a spreading subcutaneous pyoderma, the skin should not be sutured until the wound is covered with healthy granulations. In most of the cases the residual wound soon closes spontaneously. Occasionally it is possible to have the enterostomy openings entirely closed and the patient out of bed fourteen days after the first operation.

Prevention of skin irritation from open enterostomy wounds in our experience has been best obtained by (a) air exposure of wound under a bed cage and incandescent lamp, associated with frequent drying of the skin and a thick dredging with zinc stearate power; or (b) if skin has not been irritated, the cementing of a sheet of rubber dam with an appropriate hole cut in the center, to the abdominal wall with a nonirritating rubber cement. In any case ointments, oils, or retentive or macerating dressings should not be used.

Decompression of the bowel in case of obstruction is essential before any attempt is made to liberate or remove the diseased section. With the distention of obstruction, the bowel becomes permeable to bacteria, a peritonitis results which may be exacerbated to death if any extensive intraabdominal manipulation is then attempted. The obstruction is often precipitated by cathartics or heavy residue in the diet and frequently may be relieved by continuous duodenal and rectal aspiration drainage, or if there is no improvement within six hours, an appendectomy or enterostomy should be done. An appendicostomy on a thin patient necessitates only a one or one and one-half inch muscle splitting incision. No sutures or ligatures are used; dressings are applied around the exteriorized appendix and mesoappendix, the tip then cut off and a small catheter threaded into the cecum. By repeated injection and aspiration of saline, the colon then can gradually be decompressed. Daily, the indwelling catheter is replaced by one of larger size so that by the end of a week a 26 or 28 rectal tube is in place. Unfortunately, many appendices after middle life are too small to be thus used, and the side of the cecum should then be drawn through the incision, clamped, surrounded by gauze and a tube sutured in place. After the decompression it is wise to wait about three weeks for the peritonitis to completely subside before the final operation.

The Mikulicz operation may occasionally be used for rectosigmoid growths, where there is a fairly long rectum. After free mobilization to the pelvic floor, the diseased segment is removed. The distal end of the bowel should be held securely above the skin level in a strong clamp (as in the obstruction sigmoidoscopy) and into the proximal end of the bowel a bulbous glass drain is tied. Care should be taken not to incur such tension upon the loop as to cause the bowel to snap back into the pelvis before supporting adhesions have formed. A week

be more or less freely divided. Such incisions carried forward from the lateral border of the erector spinae give excellent access to deeply attached and rather inaccessible portions of the colon, leave a strong well innervated abdominal wall and, without additional incision, are convenient for the exteriorization of the deeply attached bowel, or a colostomy.

Leakage after intestinal anastomosis has been a common cause of death. Interference with the blood supply, the fatty encasement of the colon, inadequate methods of suture, back pressure, and infection have led to many preventable fatalities from this cause. Peritoneal vaccination is of little avail when the peritoneal cavity is inundated with intestinal contents, and the usual drains are quite inadequate. We have therefore resorted to very large (2.5 to 6 cm.) glass tube (lamp chimney) drains with well-rounded lower edges, which in case of doubt are anchored over the suture line (as in an ileotransversostomy) with fine alloy steel wire sutures. If the suture line breaks down, the flood of intestinal contents has then free passage externally. If inspection shows the tissue to be alive and progressively healing, the anchoring sutures are cut and the tube slipped out two to four days after the operation.

Sutures should give adequate water tight coaption without devitalization or undue tissue reaction. Catgut is unreliable as to duration of support, favors adjacent necrosis, and when used for the inner row, should be reinforced by an outer row of silk or fine alloy wire. The wire is least irritating even in a septic field. No absolutely aseptic method of suturing the colon or ileum has yet been devised, although many, such as with the Rankin or Furniss clamp eliminate gross contamination. Bacteria are forced through the intestinal wall by the compression of clamps and are carried from mucosa and Peyer's patches by sutures.

IMPROVEMENTS IN THE MIKULICZ OPERATION

We have been able to reduce the mortality and morbidity of this operation by (a) suturing the *antimesenteric* sides of the arms of the loop to avoid inclusion of mesenteric blood vessels, a cause of fatal necrosis of the bowel; (b) closing the wound about the exteriorized loop of bowel, applying dressings and immediately cutting away the diseased bowel; (c) tying bulbous glass tubes in the protruding ends of the bowel external to the skin level, to avoid obstructive symptoms and pressure perforation into the peritoneal cavity from indwelling glass or rubber tubes; (d) division of the spur by incision with immediate follow-up suture of the margins with interrupted 35 gauge alloy steel wire sutures, eight to fourteen days after the first operation. This requires no anesthetic or special preparation and saves the patient the days of discomfort occasioned by the crushing clamp; (e) the inversion

opened during attempts to free the diseased bowel. Septic areas from malignant ulceration are not infrequently opened during the operation, while cancerous tissue that appears uninfamed often contains virulent streptococci or other microorganisms. Most of these dangerous complications which raise the *general mortality* from resection of the colon to 18 or 20 per cent, may with experience be anticipated and avoided. However, when for these extensive operations aged and debilitated patients and those who have local evidence of the cancer for a year or more are included, a mortality of at least 10 per cent may be expected.

SUMMARY

Attention is directed to the advantages of a type of a single stage abdominoperineal proctosigmoidectomy with perineal colostomy or perineal anus, which may hospitalize the patient only two or three weeks. Peritonization of denuded areas in the abdomen and the formation of a pelvic diaphragm of peritoneum have been found to be unnecessary. The chief cause of death is peritonitis resulting from the spread of bacteria from infected tissue about the cancer, and especially the dissemination of bacteria through retained avascular and necrotic bowel, measures to avoid which are mentioned.

In anastomosis of the colon there is need of the more enduring silk or alloy wire sutures and questionable suture lines should be guarded by overlying "lamp chimney" drains.

Oblique muscle splitting incisions are of great advantage in many of the Mikulicz type of resections. The exteriorized loop is best removed at the first stage and tubes tied into the ends of the bowel should remain external to the level of the skin. Incision with follow-up wire suture should supplant the clamp in division of the spur as this enables the bowel ends to be united early and painlessly, saving the patient much discomfort and hospitalization. A modification of the Mikulicz operation may be used for high rectosigmoid growths with the advantage of preserving the normal sphincteric control.

1720 SPRUCE STREET

DISCUSSION

DR. LEWIS F. SMEAD, TOLEDO, OHIO.—Very practical improvements have been made in the last few years in the surgery of the colon. We have learned that we must not do radical surgery during acute obstruction; that the circulation of the colon is easily destroyed and proper care must be taken for its preservation; that infection is especially dangerous in these cases and must be avoided by some operative technic which will prevent contamination, or by some form of immunization against the infection; that there must be a careful selection of patients submitted to such radical surgery and that preoperative preparation and postoperative care must be thorough and painstaking; and finally that only very radical surgery will cure carcinoma of the large bowel.

or more later the spur is divided and sutured and when local conditions permit, the intestinal opening completely closed with interrupted sutures of fine alloy wire.

For advanced inoperable carcinoma, we find colostomy rarely desirable. By restricting the patient to a nonresidue diet, by avoiding drastic cathartics, by the use of mineral oil, enemas, and a resort to duodenal and rectal siphonage if obstruction develops, the necessity for the operation may usually be avoided. For the patient who is completely obstructed and at the most has only a few weeks to live it is, as a rule, better to let him die obstructed than to render him more repulsive and a greater burden to himself and friends through a colostomy. In the earlier stages when small irremovable metastases are present in the liver or lymphatics, the radical removal of the diseased bowel without colostomy is often a preferable operation. Several of our patients with hepatic involvement have lived from one to three years in relative comfort after removal of the primary tumor.

Peritoneal vaccination to develop more or less immunity to bacterial contamination before resecting the bowel, has been largely used, especially at the Mayo Clinic, where injections of killed streptococci and Bergen's bacillus were first advocated by Rankin and Bergen. While still employed in this clinic Rankin has in recent years expressed doubts as to its value. It is our impression that the mixture devised by Steinberg may have a greater value. There seems to be little question that complete recovery from a previous peritonitis resulting from colonic obstruction, intestinal leakage, or a previous operation markedly reduces the danger of a fatal postoperative peritonitis.

MORTALITY

The mortality from the resection of the large bowel has largely been due to sepsis, the result of leakage, or bacterial dissemination, and hemorrhage. Leakage is a common factor, having as its chief cause an arrest of circulation and secondary necrosis in the retained bowel. Death has occurred from sewing the mesenteric borders of the two arms of the liberated loop of bowel together and thus occluding nutrient vessels. Avascular as well as obstructed portions of the intestine are permeable to bacteria and stagnant blood affords a culture medium in which the bacteria may colonize before swarming out to overcome the peritoneal defenses. Such conditions are especially favorable for pathogenic activity of the *Bacillus Welchii*. Intestinal suture lines, especially in the colon, not infrequently separate followed by flooding of the peritoneal cavity with feces. An end of exteriorized bowel may retract within the abdomen and leak, an indwelling rectal or Paul tube may produce pressure necrosis, perforation, and free leakage. Intestinal clamps often squeeze bacteria through the wall of the bowel. Cancerous tissue is brittle and easily

In order to get some operability and mortality figures upon the combined abdominoperineal operations, I took 100 consecutive cases as they came into the office for examination, starting with July 1 of this year and going back. Ten of these patients went elsewhere for their operation, possibly because I would not do an operation with a perineal anus. There were 20 cases in which I thought it was impossible to remove the growth or where there may have been a metastasis in the liver. That left 70 patients who went to the hospital for operation. They were explored. Ten patients had liver involvement; 3 were inoperable on account of fixation, so that we had 57 completed operations out of the 70 cases. Of the 57 patients there were four deaths (7.2 per cent). Of the 4 deaths only two were due to peritonitis. Judging from the reactions that I have seen following peritoneal vaccine, I would hate to submit 70 patients to the reaction from intraperitoneal vaccination.

DR. BABCOCK (closing).—Impressed by Steinberg's demonstration at our Toledo meeting, I returned with samples of his colibactragen which we have used in a few cases. One result was particularly gratifying. The bowel in this particular case had given way and the peritoneal cavity flooded with fecal material. An associate who was operating poured the bactragen into the cavity and the patient recovered without untoward symptoms.

The one stage proctosigmoidectomy we have described does not sacrifice any radical quality. In some ways it is more radical than the conventional operation with an abdominal colostomy.

As to the mortality we have not as yet equaled the splendid record of Dr. Jones. Taking all cases it has been about 18 per cent, because we have included advanced cases with perforation and perirectal infiltration, recurrent cases and especially because a technic to insure routinely viable bowel to the pelvic floor was not developed early. Eliminating those cases in which septic areas were invaded and those in which through technical error the blood supply to a section of the retained sigmoid had been arrested, the mortality has been well under 10 per cent, and as a rule the convalescence has been very rapid and surprisingly easy. It is evident, however, if the operator fails to free a section of well vascularized sigmoid long enough to reach from the pelvic brim to the pelvic floor (12 cm.), he should finish the operation with an abdominal colostomy.

As to the Mikulicz method for the removal of carcinoma near the rectosigmoid junction, it is to be remembered that the unstretched rectum alone is 12 to 15 cm. long, while the anus measures 3.5 cm. additional. Under traction the pelvic floor is raised and the rectum elongated. Therefore, cancer situated about the level of the pectineal line after the rectum has been freed, may often be lifted through an abdominal incision with 5 to 8 cm. distal bowel to spare. Thus we have been able to leave a number of these patients with a normal perineal anus.

It is well recognized that in operations subsequent to colostomy the peritoneum is not easily infected. It has therefore been the hope of surgeons that this immunity could be produced artificially. Numerous attempts have been made to bring about such an immunity, chiefly by the intraperitoneal injection of bacteria suspended in saline solution. This process takes at least two or three weeks and produces a moderate degree of immunity but only against the type of bacteria injected. It is essential in this connection to understand that the cause of death in peritonitis is the absorption of toxins produced by bacteria while they are within the peritoneal cavity. The bacteria which reach the blood stream from the peritoneal cavity are usually very quickly destroyed, chiefly by the fixed phagocytic cells of the reticulo-endothelial system. The problem then is to develop some general form of protection which will really be efficient against all types of bacteria which may cause acute peritonitis. The phagocytic cells of the blood would seem to offer such a general protection, for they are no respecter of persons and will destroy one organism as well as another. The difficulty has been to get the phagocytic cells into the peritoneal cavity in sufficiently large numbers at the opportune time.

When dead colon bacilli suspended only in saline solution are injected into the peritoneal cavity, phagocytic cells are called out but in insufficient numbers, due to the fact that the colon bacilli remain in the peritoneal cavity too short a time. However, Steinberg found that virulent, killed, colon bacilli suspended in 1.5 per cent gum tragacanth solution were retained much longer in the peritoneal cavity and caused it to be flooded with huge numbers of phagocytic cells over a period of some three days. This has protected animals against massive fecal contamination of the peritoneal cavity which was always fatal to the control animals.

This suspension of colon bacilli in gum tragacanth solution (colibactragen) is used in clinical work by spreading it freely through the peritoneal cavity at the end of an operation in which contamination is suspected. The phagocytic cells are present in large numbers within three hours thereafter while the infecting organisms require some eighteen hours to multiply sufficiently to cause trouble. However, long before this most of the bacteria will have been taken up by the phagocytes and are harmless. The cell count of phagocytes in the peritoneal cavity will show a minimum of 90,000 per c.mm. in three hours with a maximum of 450,000 in twelve hours. The clinical results in a considerable number of cases in the hands of several good surgeons have been striking and quite convincing. The earlier preparation, given out for clinical trial, gave severe reactions but the material as now prepared gives very little reaction and acts more quickly.

DR. THOMAS E. JONES, CLEVELAND, OHIO.—There are three serious objections to Dr. Babcock's operation; first, there is danger of interference with the blood supply; second, if one constantly has to worry about the blood supply, there is a tendency to the removal of too little tissue; and third, a large raw surface not peritonized is left in the pelvis.

The chief difficulty from the abdominal colostomy has existed because the surgeon has not taken time to instruct the patient in its care. In the cases I have observed with perineal anus on the other hand there has either been a stricture or too large an opening, with prolapse of the mucous membrane. If the latter occurs there is a lot of mucous discharge, which is very irritating to the perineal skin and requires the patient to wear a perineal pad constantly. Patients who are constricted frequently require dilatation.

Dr. Babcock showed a slide of the Mikulicz procedure for rectosigmoidal carcinoma. I look upon the rectosigmoid not as an area or length of bowel, but simply the point at which the rectum joins the pelvic colon. It is certainly not two inches above the reflection of the peritoneum, and it is impossible to bring that out on the abdominal wall and do a Mikulicz operation.

five daily injections of antuitrin-S. The flow became scant but irregular spotting continued until she was seen on July 27, 1934. She was advised to have a diagnostic curettement but delayed until Oct. 16, 1934 (Fig. 1). The spotting continued during that time. When curetted at that time the cervix was soft and dilated easily. The uterine sound showed the depth of the uterine cavity to be 7 cm. Manipulation with the sound induced bleeding. The curette demonstrated a small submucous fibroid. Some clots and a small amount of endometrial tissue were removed. Frozen sections showed no malignancy but Dr. Hartman reported that the fixed sections of the endometrium seemed to be the seat of a very marked papillomatous growth which should be considered early or borderline malignancy, because of the variation in the size and shape of the cells, and because of the marked activity (Fig. 2). Many of the cells showed clear vesicular nuclei. Mitotic figures were present but not

*108422 Mrs. S.D.

AGE 44. MENSTRUAL HISTORY. REGULAR 25 DAY AVERAGE

ONSET. 13 INTERVAL. 25 DAYS

PAIN ++ DURATION. 3 DAYS AMT. AVERAGE

SAMPLE CHART

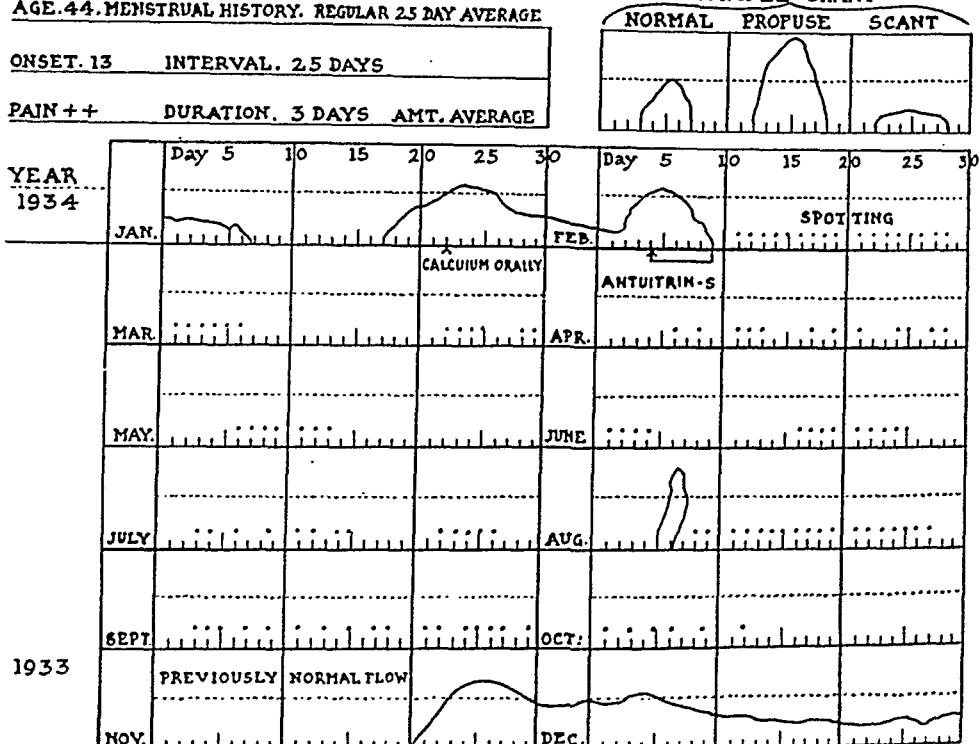


Fig. 1.—A chart given to patients to obtain a graphic record of their menstruations. The sample in the upper right corner is explained to the patient to indicate the method of charting. The dotted line indicates the height of an average amount of flow. The curves drawn on the chart indicate the interval and amount of flow. The dots indicate spotting. This particular chart began in November, 1933 and ended October, 1934. The time of administering medication is shown. While the chart is not scientifically accurate it provides a more accurate record than can be obtained from the memory of a patient. Preceding records by the patient were nearly normal until November, 1933. This was the first metrorrhagia and the first flow continuing longer than seven days.

abundant. There was a great deal of blood but little or no stroma. Radium (4500 mg. hr.) was given. The uterus atrophied. All discharge ceased. There has been no further evidence of the presence of malignancy.

CASE 2.—M. N., a single teacher, fifty-eight years of age, has an important family history because her mother, one sister, and an aunt died from cancer. Her menstruations began at fourteen years of age. The first period was accompanied by a convulsion. She always had dysmenorrhea. The flow was irregular with an interval up to five weeks but usually every twenty-one days. The flow was usually

EARLY DIAGNOSIS OF CANCER OF THE BODY OF THE UTERUS*

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THE earlier that cancer is diagnosed the greater the chance of cure. Bleeding is recognized as the most common symptom of cancer of the body of the uterus. Closer observation of the character of bleeding at and after the menopause by the patient, and more careful interpretation of the significance of the bleeding by the physician, offer an opportunity for early diagnosis. Two case reports illustrate the benefit to be derived from the cooperation of the patient and physician. A third case illustrates the association of hyperplasia and carcinoma.

Placing emphasis on bleeding does not exclude the importance of other symptoms and examinations. Education of the public through the press and by lectures has focused the attention of women on irregularities of bleeding. An explanation for unusual bleeding is now frequently sought where formerly it was assumed to be a part of the menopause. This is especially fortunate for the cases of cancer occurring near the menopause.

CASE REPORTS

CASE 1.—Mrs. S. D., forty-four years of age, was slightly obese. The family history was not important. There was no history of cancer. She was married but had never been pregnant. Her menstruations had been essentially normal with an average amount of flow occurring about every twenty-eight days. In May, 1933, she came to the clinic for a general examination because she had headaches, dizziness, low back pain, abdominal distress, constipation, and leucorrhea. For several months there had been some irregularity of menstruation with a prolonged interval followed by a shortened interval and profuse flow. Correction of ametropia relieved the headaches. The low back pain was explained by mild arthritis. The abdominal distress and constipation was accounted for by a functional nervous disturbance with pylorospasm. The leucorrhea was explained by a slight erosion of the cervix. The uterus showed beginning involution and a small fibroid. She was given a chart to record the character of her menstruation (Fig. 1). On account of a subacute bronchitis and ethmoiditis she was treated in another department for the next few months. In November, 1933, there was a profuse flow continuing until Jan. 5, 1934. Calcium was administered orally with some improvement but the flow remained heavy until she returned Feb. 2, 1934. At that time she received

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Photomicrographs prepared and diagnosed by Dr. Frank Hartman, Chief of Laboratories, Henry Ford Hospital.

and demonstrated that the blood came from the vagina. On Nov. 25, 1933, vaginal examination showed no gross discharge or blood. In view of the patient's family history and her demonstration of the blood having come from the vagina, the vaginal cavity was washed with normal, salt solution. The sediment from this washing



Fig. 4.—Photomicrograph, medium power: section from uterine mucosa showing single uterine gland and carcinoma. The carcinoma is composed of irregular atypical alveoli and solid masses of cells.



Fig. 5.—Photomicrograph, medium power: uterine mucosa shows irregular hyperplastic glands and solid masses of anaplastic cells representing undifferentiated adenocarcinoma.

showed many red blood cells. The small vagina made it difficult to examine the cervix and she could not tolerate manipulation of the cervix without an anesthetic. A curettement was advised.

On December 9, the uterus was curetted. The fundus was not enlarged. Slight bleeding followed dilatation of the cervix. A small amount of material was removed

scant sometimes lasting only one day. Menopause occurred at age of forty-eight years. During the summer of 1933, she noticed a slight yellowish, irritating discharge, probably due to trichomonas infestation. It disappeared promptly after taking douches. During the summer of 1933, she noticed a few specks of blood which were assumed to be from the rectum. She gave a history of a thrombosed hemorrhoid. Nov. 14, 1933, a routine pelvic examination revealed normal involution

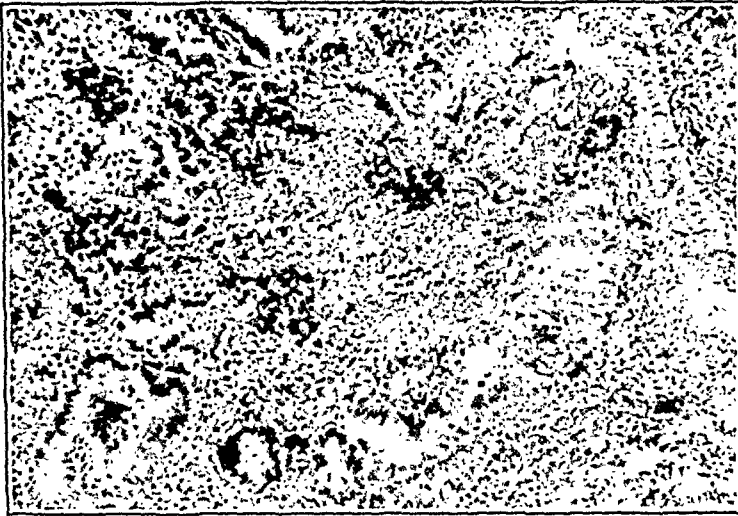


Fig. 2.—Photomicrograph, medium power: section of uterine mucosa removed with a curette, showing irregular atypical glandular alveoli lined by several rows of large columnar cells. The nuclei are hyperchromatic and many of them are undergoing mitosis. In addition to the tumor, there is much blood in this section.

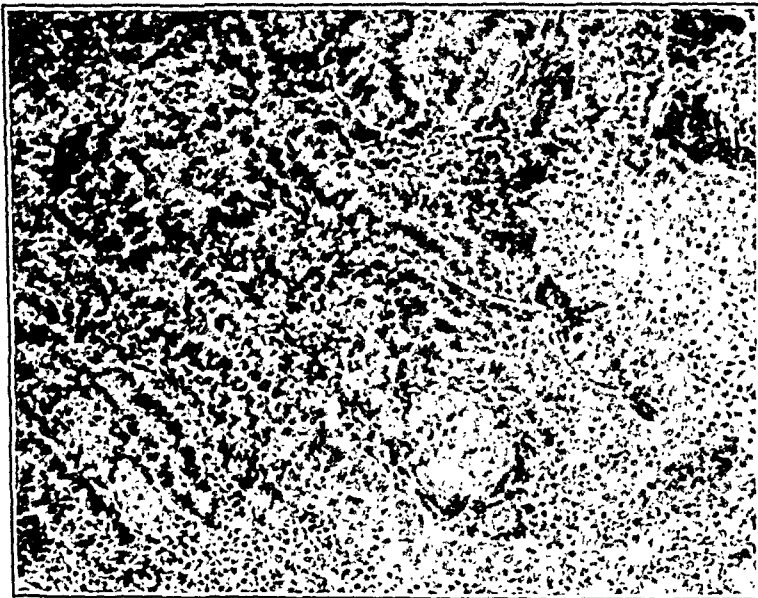


Fig. 3.—Photomicrograph, medium power: section from uterine mucosa removed with curette. Sections show atypical tubular glands lined by several rows of high columnar epithelium. Individual cells are large, having hyperchromatic nuclei and many of them undergoing mitosis.

of the uterus, a normal cervix, no vaginitis, and no discharge. In view of the hemorrhoids and bleeding, a proctoscopic examination was done but nothing found except the hemorrhoids and a small, rectal polyp. She was given local treatment for the hemorrhoids. During the following week the patient continued to notice slight blood stains on her clothing. The patient made some examinations on herself,

Other types of charts might be equally effective. This one (Fig. 1) is easily understood by an intelligent patient. Explanation of the sample in the upper right hand corner with a statement that the dotted lines represent the height of an average amount of flow enables the patient to produce an informative record. The data obtained in this manner are more reliable than vague statements by the patient according to her recollection. Keeping the record fixes the attention on obtaining accurate data. Many instances are recorded that otherwise would soon be forgotten. Failure to return the chart usually means that the record is essentially normal. Review of the chart with the patient tends to allay her fears rather than to create fear.

In the interpretation of irregularities of bleeding during the menopausal period, continuous flow whether small or large is particularly significant. Continuous flow may be considered a definite indication for diagnostic curettement. Irregularity in the interval or amount of cyclic flow during the premenopause is common. Transition from the cyclic to continuous flow should always arouse suspicion. Adequate standards for the normal cycles during the premenopausal period have not been established, therefore, aberrations of flow are difficult to define. Failure of the cyclic nature of the flow cannot be considered normal. Hot flushes and other symptoms which establish the diagnosis of the menopause do not justify attributing bleeding to the menopause and excluding the possibility of the presence of malignancy. Cessation of bleeding following the use of calcium or antuitrin-S for any considerable period is not expected if malignancy is the cause.

The relation of hyperplasia of the endometrium to adenocarcinoma of the body of the uterus is often difficult to determine. Bleeding is a symptom common to both lesions. The frequent occurrence of abnormal bleeding near the menopause complicates the clinical diagnosis and demands an explanation. The most experienced pathologists find difficulty in classifying the borderline cases. Whether both lesions exist in the same uterus is controversial. Reports in the literature vary from a high percentage (Novak) to none (Burch). Definition of what constitutes hyperplasia explains some of the differences of opinion concerning the relation of hyperplasia of the endometrium to cancer.

Novak and Yui reviewed 12,813 specimens of endometrium among which they found 804 hyperplasias and 104 adenocarcinomata. Among the 804 cases, 14 revealed "evidence of proliferative tendencies which may even simulate cancer." In 40 of the 804 cases, hyperplasia was found long after the menopause. Coexisting hyperplasia was found in 25 of the 104 adenocarcinomata. They maintain that the persistence and relative excess of estrone predispose to cancer.

with the curette. Microscopic examination of the curettings showed numerous atypical glands separated by a very small amount of stroma (Fig. 3). The glands varied in size. The cells were large and irregular with numerous mitotic figures. The lining cells were more than two layers thick in places. The stroma showed some infiltration, and in some places the cells were grouped in solid masses but in general, an alveolar arrangement was maintained (Fig. 3). The diagnosis was adenocarcinoma of the fundus, Type II. Radium (6,000 mg. hr.) was applied. On Jan. 11, 1934, hysterectomy was performed. The endometrium showed degenerative changes in response to the radiotherapy. In February, deep x-ray therapy was given. There has been no evidence of return of the growth.

CASE 3.—Mrs. M. B., aged sixty-five years, passed the menopause at the age of fifty-two years. Her complaint, on admission, was vaginal bleeding. After the sudden cessation of menstruation at the age of fifty-two, there had been no further bleeding until the age of sixty-four. During that year she had experienced spotting. For three weeks prior to admission, she had continuous flow with two severe hemor-



Fig. 6.—Photomicrograph, medium power: section from uterine mucosa shows cystic glands lined by low columnar epithelium, and in one instance containing pink staining debris. In addition there are hyperplastic glands which are relatively small and lined by several rows of high columnar epithelium.

rhages. During this time there was an associated vaginal discharge. A preoperative diagnosis of carcinoma of the fundus was made from the history and the enlargement of the fundus. Hysterectomy was performed and the diagnosis confirmed. Photomicrographs showed typical anaplastic adenocarcinoma (Fig. 4), transitional areas of hyperplasia of the endometrium (Fig. 5), and hyperplasia in an atrophic endometrium (Fig. 6).

DISCUSSION

The value of a graphic record of menstrual irregularity during the menopause is illustrated by Case 1. The record was requested as a part of a study to determine the normal limits of irregularities of flow during the premenopause and through the menopause. At the time the chart was started, there was no suspicion of malignancy and probably one existed, since the specimen obtained later showed a very early malignancy.

frequent association of two or more of these conditions necessitates consideration of all of them in each case observed. Any bleeding after the menopause should be regarded as malignant in origin, until proved otherwise. Before the menopause, the indications are not so well defined but metrorrhagia is particularly significant.

Late menopause is emphasized by Crossen and Hobbs for its frequent occurrence preceding adenocarcinoma of the fundus. Of 56 cases of adenocarcinoma, 60 per cent of the patients passed the menopause at fifty or later, while only 15 per cent of the normal patients had a menopause as late as fifty. In their series, therefore, the incidence of late menopause in cases of adenocarcinoma of the fundus was about four times as high as in the normal cases. They were not able to obtain satisfactory statistics regarding the frequency of adenocarcinoma in late menopause. Nevertheless, they maintain that late menopause is a warning of a tendency to malignancy.

In reviewing 71 cases of adenocarcinoma of the body of the uterus, I found 40 (56 per cent) postmenopausal. The time elapsing between the menopause and the appearance of carcinoma varied from two to twenty-eight years with an average of thirteen years. Among the 40 postmenopausal carcinomas, the age of cessation of flow was earlier than fifty years in 23 cases or 57 per cent, and later than fifty years in 17 cases or 42 per cent. The average age of the menopause was 47.8 years. In this small group, the late occurrence of the menopause bears no significant relation to the incidence of carcinoma.

When curettement for diagnosis is indicated, two things should be emphasized. First, the procedure should be thorough in order not to miss an early lesion. Second, frozen sections of suspicious pieces of tissue are inadequate (Case 1). All of the material obtained should be collected and enough sections cut to insure inspection of all fragments of the curettings.

Improvement in the cure of carcinoma depends largely on the education of the laity. The physician cannot diagnose until the patient seeks his advice. Much has been accomplished by inducing women to report for periodic examinations. Interest has been stimulated in irregular bleeding. The graphic chart presented here is another means of increasing this interest and obtaining the cooperation of the patient. Furthermore, the chart improves the accuracy of the record and facilitates the interpretation of the bleeding.

SUMMARY

1. Bleeding is the most common symptom of adenocarcinoma of the body of the uterus, having been present in every one of our 71 cases.

2. Three case reports illustrate: the importance of irregular premenstrual bleeding; the significance of postmenopausal microscopic bleeding; and the association of adenocarcinoma and hyperplasia.

In reviewing 594 specimens of hyperplasia, Payne found 13 carcinomata. In 496 premenopausal hyperplasias he found 8 carcinomas (1.6 per cent), with only 1 cervical carcinoma (0.2 per cent). In 38 postmenopausal hyperplasias there were 4 carcinomas of the fundus (11 per cent).

In 152 cases of adenocarcinoma, Taylor found 15 with definite histologic evidence of an associated hyperplastic condition of some type, but he believes that one cannot speak in terms of percentages, since it is obvious that many cases are so advanced that possible benign preexistent lesions have been completely displaced by carcinoma. In his series, he noted 5 instances of diffuse endometrial hyperplasia associated with carcinoma.

Opinions differ concerning the association of myoma and adenocarcinoma of the uterus. In general, carcinoma is found more frequently in the myomatous than in the normal uterus.

Oesterlin and Cron cite some of the cases reported in the literature. Among their own cases, they found in 17,030 tissue examinations that 531 or 3 per cent concerned myoma. Fundal cancer and myoma were found together in 10 cases or 1.9 per cent of all myomas. The 10 cases represented 25 per cent of the fundal cancers. Compared with fundal cancer, they found myoma associated with cervical cancer in only 0.19 per cent.

The presence of myoma in a uterus offers some difficulty in excluding a diagnosis of carcinoma. Bleeding resulting from preexisting myoma may mask the symptoms of carcinoma. The myoma may obstruct the uterine cavity to make a thorough curettement difficult or impossible. The absence of carcinoma in the curettings should not be taken as final proof that carcinoma is not present.

The occurrence of carcinoma in endometrial polyps has been frequently reported. Bleeding is a common symptom of uterine polyps. Benign and malignant polyps may exist in the same uterus. Removal of a single polyp should be followed by a thorough curettement to exclude other polyps.

Bleeding is the most common symptom of adenocarcinoma of the body of the uterus. Review of the clinical records of 71 cases indicated the presence of bleeding, varying from microscopic to gross in every one of them. The character of the bleeding differs in the pre- and postmenopausal patients.

In a review of the literature, Wittenbourg and Zlatmann found that the incidence of postmenopausal bleeding due to cancer ranged from 26 to 92 per cent. In their own cases, 41 per cent was due to cancer of the uterus or ovary, while only 7 per cent was due to benign tumors. Of 1,797 cases of uterine hemorrhage occurring before, at, or after the menopause, Norris reported 20 per cent due to malignant tumors. Of the postmenopausal hemorrhages, 52.9 per cent were due to cancer.

The amount of the bleeding is not an accurate indicator of the extent of the lesion. Case 2 shows the importance of observing microscopic bleeding. The common causes of bleeding during the cancer age, besides carcinoma, are myomas, hyperplasia and polyps. The

taking place. Another patient was convinced that a profuse hemorrhage came from the vagina when really it had come from the bladder, due to an essential hemorrhage of the kidney.

Diagnostic curettage with microscopic examination of the fragments may prove misleading. At the present time two such cases are in my wards. One had had a recent curettage by another surgeon and had been assured that the pathologic examination showed nothing dangerous. Her symptoms were so suggestive of corpus cancer that I removed her uterus which showed a well-marked malignancy of the fundus. In this case either the previous curetting had not been thorough or the interpretation of the sections had been faulty. In the other patient, uterine bleeding at the age of sixty-four years was the only symptom, and pelvic and abdominal examination showed nothing abnormal. Thorough curetting of the small atrophic uterus produced insufficient tissue for microscopic diagnosis. Continued bleeding led to an exploratory section which revealed a widespread abdominal carcinosis with secondary nodules in the liver and extensive involvement of the omentum. A small secondary growth involved one tube and mesosalpinx, and this was evidently the source of the bleeding into the uterus which showed no involvement itself. Exploratory operation would therefore seem justified in continued postmenopausal bleeding, even if pelvic examination is negative and a diagnostic curettage shows no certain malignancy.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—In cases where there is good reason to suspect malignancy a special request should be made to the pathologist to block all of the curettings and to cut sections from many different levels of the block. It is also important for the clinician to know that the curettings represent all of the uterine mucosa, otherwise he is not justified in judging that the pathologist has failed to make a positive diagnosis.

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—There were 150,000 patients who died of carcinoma in the registration area of the United States during 1935. Of this number, 82,000 were women and 50 per cent of the women died of carcinoma of the female generative tract. This disease is increasing at such a rate that we must give more consideration to the signs and symptoms of malignancy of the generative tract in women.

I have yet to see a carcinoma of the fundus in which there was not a failure or inactivity of the corpus luteum. I am certain that carcinoma of the fundus is definitely connected with the physiologic chemistry of the corpus luteum. If it occurs before the menopause it affects the woman who has a very irregular menstruation, which is the result of ovarian dysfunction.

No one has said whether the treatment should consist of roentgen therapy, radium therapy, or operation. Personally, I feel that inasmuch as 95 per cent of the carcinomas of the fundus grow very slowly and therefore are resistant to radium, and since carcinomata of the fundus respond especially well to surgical treatment, they should be treated by total hysterectomy.

DR. MORTIMER N. HYAMS, NEW YORK CITY.—I would like to ask the essayist if he has had any experience with uterosalpingography as an aid in the diagnosis of early carcinoma of the fundus of the uterus. It has been our custom at the New York Postgraduate Hospital to use the serial or fractional method of hysterosalpingography. This method consists essentially of successive injections of 2 c.c. each of a contrast medium with x-ray exposures after each injection until a total of 10 c.c. has been reached. The lumen of the uterine cavity and the Fallopian tubes is gradually outlined, and any defect in contour delineated step by step.

This method is particularly valuable in the diagnosis of obscure uterine conditions in women between thirty-five and forty-eight years of age, who present

3. A chart is presented which stimulates the interest of the patient in bleeding, provides a graphic record, and aids in the interpretation of premenstrual bleeding.

4. Examination of a single fragment of tissue is inadequate. Sections from all the curettings should be studied.

5. Early diagnosis of adenocarcinoma of the body of the uterus depends upon the education of the laity to observe and report all irregularities of premenopausal bleeding and all postmenopausal bleeding.

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DISCUSSION

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—In the pathologic laboratory at the Syracuse Memorial Hospital, all curettings are "put through," there being at times as many as ten or twelve blocks. I never feel confident in frozen sections of uterine curettings. For example, I was asked to make a frozen section of curettings on a patient about to have an interposition operation. I picked several pieces which when cut showed benign hyperplasia. Permanent sections showed a definite adenocarcinoma accompanying the hyperplasia. When these slides were examined twenty-four hours after operation, the patient had already had the interposition operation done.

The question of responsibility in the early recognition of cancer is pertinent. We have criticized the public for not appearing early. We must also criticize a good many members of our profession for not giving the patient a thorough and complete study when she does appear.

DR. W. A. SCOTT, TORONTO, CANADA.—Four cases have been encountered in a study of our carcinoma cases that emphasize a point not mentioned this morning. These patients had all been submitted to previous diagnostic curettage, one five years before, all of them more than one year before. We feel that in each this previous curettage was done very thoroughly. Subsequently each patient again developed irregular bleeding. Having been submitted to diagnostic curettage once and told that they did not have carcinoma, the symptoms were neglected with the onset of the next bleeding.

The members of this society know what is meant by thorough curettage, but the general practitioner sometimes does not. We know that carcinoma begins in the cornua of the uterus sometimes and that is the most difficult point from which to obtain a specimen. We are entirely against any such thing as aspiration for a diagnosis of fundal carcinoma. Although a frozen section may be of use, if it is positive, it is of very little use if it is negative, and we feel that all of the curettings should be examined in paraffin sections and done very carefully.

DR. WILLIAM H. WEIR, CLEVELAND, OHIO.—In cases of postmenopausal bleeding, it is very necessary to determine that the source of the bleeding is actually the uterus. One patient of mine had to be seen several times before it could be shown that the occasional hemorrhage came from a pinpoint opening in the prolapsed urethral mucosa, so small that it could not be seen unless the bleeding was actually

carcinomata of the uterus and 47 were primary and 60 recurrent cancers. Among the primary carcinomata, 10 were in the body and 37 in the cervix, and among the latter 6 were stump cancers, i.e., about 16 per cent. Thirteen of the primary cancers, namely all the corpus cancers and a few cervix carcinomata, were treated either with radium or with radium and Roentgen rays, and 34 primary cervix cancers were treated with 800 K.V. Roentgen rays without the addition of any other form of radiation. These 34 cases form the basis of this report and discussion.

THE ACTION OF 800 K.V. ROENTGEN RAYS ON CARCINOMA CELLS

The cellular changes produced in carcinomas depend to a great extent on the Roentgen ray dose applied at or in the tumor. The dose may be determined from measurements of the distribution of radiation

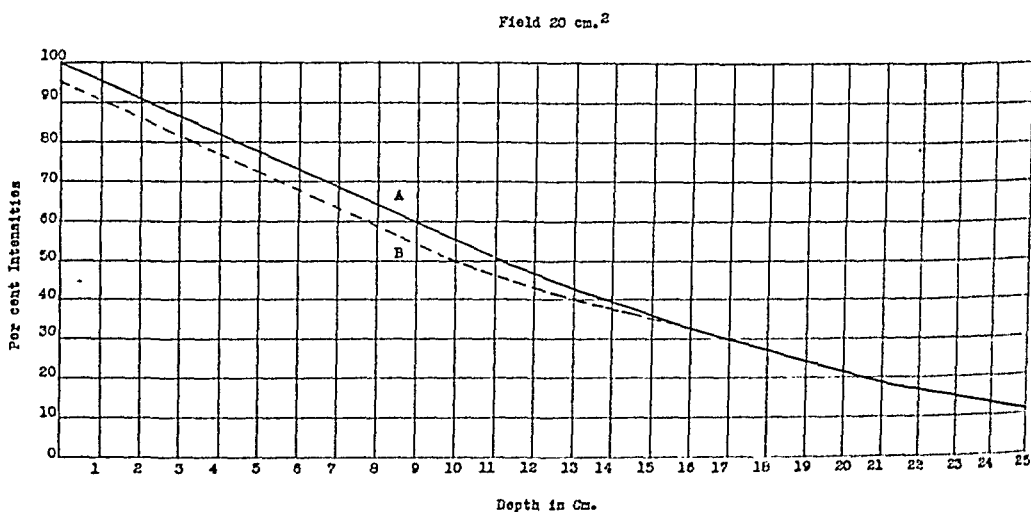


Fig. 1.—A, Absorption graph in center of field. B, Absorption graph 10 cm. lateral from center of field. One may say that the intensities at the periphery of the field are roughly 8 per cent lower than in the center until a depth of 15 cm. is reached when the intensities form a straight line.

intensities in a phantom. The latter was constructed of bakelite in such a way that the horizontal area was always 30 cm. square, but the vertical area could be changed to any desired anteroposterior diameter. In pelvic tumors the anteroposterior diameter was 22 cm. in more than 90 per cent of the female patients and 20 cm. or less in about 75 per cent of patients.

The graph shown in Fig. 1 was drawn from such measurements. Such a graph enables one to calculate the intensities attained in a pelvis with radiations applied through two or more ports of entry. For pelvises having an anteroposterior diameter of 24 cm. or less two fields are used. Should the anteroposterior diameter be 25 cm. or more three or four fields are given. The axis of the beams is kept at an angle of 30° from the anteroposterior axis. The patient is maintained in this position by the use of rubber bags filled with sand.

no physical findings to account for irregular vaginal bleeding. The filling defect of the submucous uterine fibroid, the uterine polyp, the irregularity of the hypertrophic endometrium, the decreased density of the intramural fibroid and the craterlike formation in carcinoma of the fundus can usually be well defined.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—I should like to call attention to the relation between uterine polyps and carcinoma. Cervical polyps are of relatively little importance as the site of malignant change, and we have, in fact, only one specimen of this type. On the other hand, malignant change is relatively common in polyps arising from the endometrium.

The great danger in the pathologic diagnosis of absence of malignancy from fragments of such polyps lies in the fact that most of the material for biopsy is obtained from the periphery of the growth; whereas the primary development of malignancy usually occurs in the pedicle or the base of the polypoid mass. This is rarely obtained by ordinary biopsy technic.

DR. PRATT (closing).—The problem of adenocarcinoma of the fundus is altogether too broad to be considered as a whole. I wanted simply to emphasize bleeding as a sign which should always be explained, and the necessity of getting the cooperation of the physician and the patient.

Diagnosis in borderline cases of adenocarcinoma and hyperplasia may be very difficult, as Dr. Sears has pointed out. A doubtful case should be submitted to a jury of three which includes a pathologist and the operator.

Dr. Counsellor has taken a position in reference to the corpus luteum that can be partly substantiated. Inasmuch as a majority of adenocarcinomas of the fundus occur after the menopause, there would be natural failure of the corpus luteum as well as many other tissues.

Uterosalingography is undoubtedly useful.

CLINICAL OBSERVATIONS ON THE TREATMENT OF PRIMARY CARCINOMATA OF THE CERVIX WITH 800 K.V. ROENTGEN RAYS*

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THE treatment of carcinomata of the uterus with Roentgen rays in the region of 800 K.V. maximum was begun May 1, 1933. Though the five-year survival rate cannot as yet be given, a report on (1) the action of the 800 K.V. Roentgen rays on the carcinoma cells; (2) the reaction of the patient to the irradiation; (3) the changes produced in the skin and mucous membranes exposed to Roentgen rays; and (4) the three- and four-year survival rate of the primary carcinomas treated from May 1, 1933 to Dec. 1, 1934, would be of interest.

During this period, 873 patients with malignant diseases were admitted to the Radiation Institute. One hundred and seven cases were

*Read at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20 to 22, 1937.

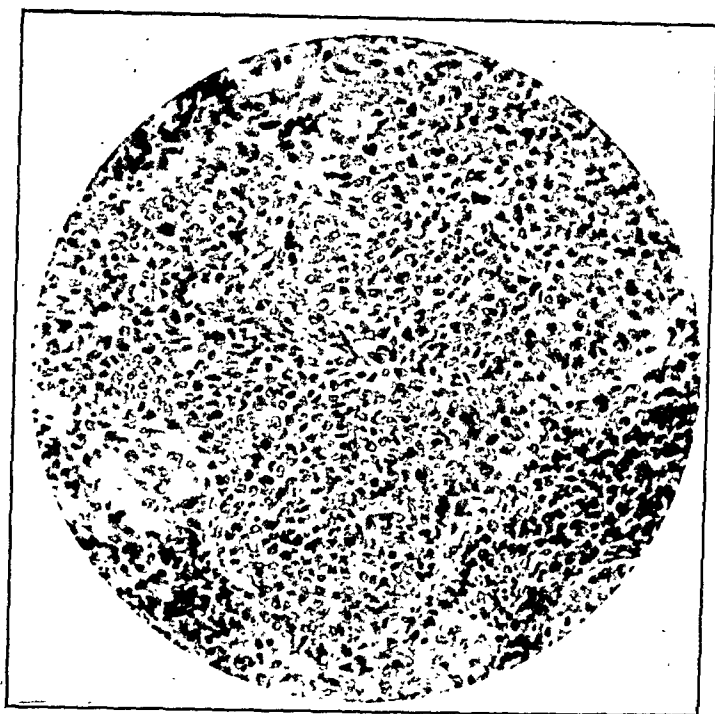


Fig. 2.—Squamous cell carcinoma (Grade II) before irradiation.

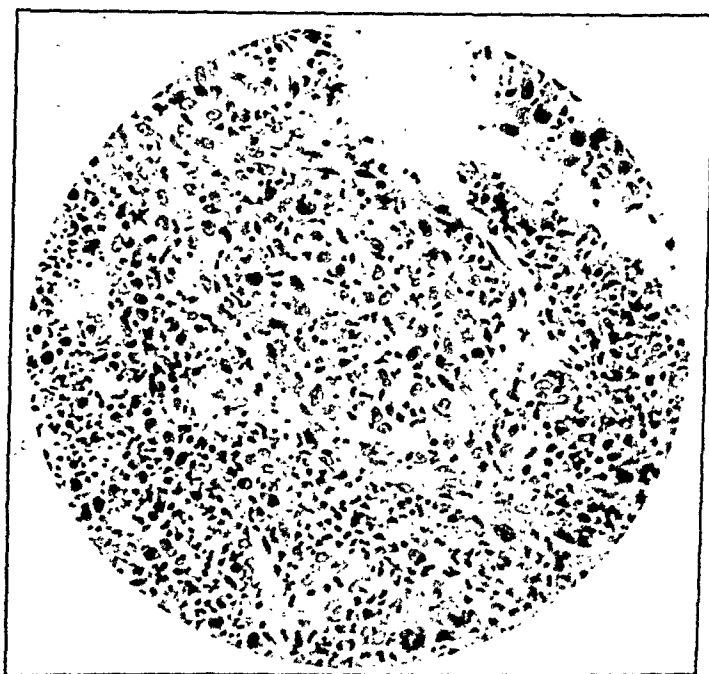


Fig. 3.—Tumor, illustrated in Fig. 2, after a tumor dose of about 1600 r. with backscatter had been given in the midpelvis. Swelling of cytoplasm and nuclei are predominating features. Magnification same as in Fig. 1.

Table I shows such a calculation for two fields.

The action of the Roentgen ray on the cellular components of the cervix is illustrated by the microscopic examination of tissues removed by biopsy. The first microphotograph, Fig. 2, was obtained from tissue before the commencement of treatment on July 1, 1937.

TABLE I. THE DISTRIBUTION OF CALCULATED INTENSITIES FROM 2 FIELDS EACH 20 SQ. CM. IN A PELVIS WITH AN ANTEROPOSTERIOR DIAMETER OF 20 CM.

DEPTH IN CM.			
0	114.3 93 + 21.3	121.3 100 ÷ 21.3	114.3 93 + 21.3
5	106.6 72.5 + 34.1	116.0 70.55 + 36.5	106.6 72.5 + 34.1
10	94.6 47.3 + 47.3	110.0 54.50 + 54.50	94.6 47.3 + 47.3
15	106.6 34.1 + 72.5	116.0 36.3 + 79.50	106.6 34.1 + 72.5
20	114.3 21.3 + 93.0	121.3 21.3 + 100	114.3 21.3 + 93.0

Pathologic Report.—Sheets of tumor epithelial cells were separated by a stroma which was less abundant than the epithelium. The stroma consisted of fibroblasts, collagen, and capillaries, and its components were difficult to define due to massive infiltration by lymphocytes and plasma cells. Both the epithelium and stroma showed numerous eosinophiles. The epithelial cells were of moderate size with nuclei of moderate size. The latter were roughly oval or elliptical in the central portions of the sheets, more columnar and elongated near the stroma. In an occasional column of cells most of the nuclei were elongated. In structure, the nuclei were rather open, knots of chromatin and occasionally a nucleolus being prominently defined. The cell boundaries in areas were difficult to define. The cytoplasm was for the most part homogeneously basophilic. Mitoses averaged 1.7 per oil immersion field ($\times 900$). (Range 4-0 in twenty fields.) Some of the mitoses were abnormal in form. In some areas the elements of the stroma were separated by clear spaces. Here the tumor cells were swollen, showing vacuolated cytoplasm and large vesicular nuclei. The cell and nuclear boundaries were at times poorly defined. No pearls or keratohyalin granules were noted.

Diagnosis: squamous cell carcinoma (Grade II).

The second microphotograph (Fig. 3) was obtained from a biopsy taken July 15, 1937 after five fraction treatments, each approximately 425 r. with backscatter, had been given. Therefore, the midpelvic dose attained was approximately 1125 r.

Pathologic Report.—There was moderate swelling of the tumor epithelial cells, the swelling predominating in their cytoplasm which for the most part was finely vacuolated. There was only moderate swelling of the nuclei. The latter were more vesicular and the chromatin masses and nucleoli were more pronounced than in the previous biopsy. There were numerous coarse vacuoles between the cells. The mitoses were fewer in number, average 0.4 per oil immersion field ($\times 900$). (Range 2-0 in 20 fields.) Those seen were abnormal. One monaster showed clumps of chromatin near distal ends of spindle in addition to normal arrangement of chromosomes at its equator. There was swelling of the vascular endothelium and a looser structure to the stroma. Many of the polymorphonuclears were pyknotic; the structure of the plasma cells in the stroma was better defined and these cells

seemed slightly larger than in the previous section. A strip of noncornified stratified squamous epithelium appeared in this section. The cytoplasm of the cells in the Malpighian layer was slightly swollen. Many of the nuclei were pyknotic, a vacuole in apposition representing the original size of the nucleus. Prickles were well defined. In one area there was vesicle formation in the Malpighian layer.

Another five fraction treatment was given, the midpelvic Roentgen dose being approximately 2250 r. The biopsy report following this treatment was: No tumor was present. Specimen consisted of fragments of normal cervical tissue and blood clot.

On July 30, 1937 following the application of another five fraction treatments and a midpelvic Roentgen dose of about 3375 r., the examination of tissue showed the absence of all tumor tissue (see Figs. 4 and 5).

Pathologic Report.—No definite tumor was noted. The specimen consisted of mucus, masses of neutrophiles, and minute strips of stratified squamous epithelium. This epithelium was definitely not cancerous and was arranged in the ordinary layers.

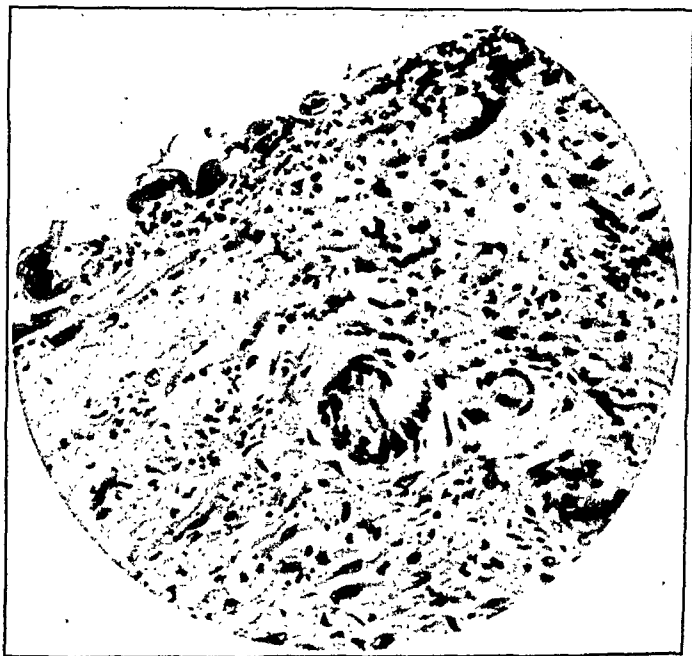


Fig. 6.—Radiation changes in noncancerous epithelium of cervix after a total of 4250 r. had been applied to midpelvis. Disappearance of most of epithelial cells with thin layer of fibrin and neutrophiles covering denuded area. Hyalinization of arteriolar walls. Proliferation of internal fibroblasts. Same magnification.

In this epithelium moderate swelling of the cytoplasm and nuclei with vacuoles in cells and between cells was noted. Prickles were still present. Hyaline globules represented remains of some of these cells. In portions of the epithelium, numerous large vacuoles filled with neutrophiles were noted. There were no mitoses (see Figs. 4 and 5).

A biopsy taken on Aug. 6, 1937 at the completion of the Roentgen treatment, and seen in Fig. 6, showed the changes accompanying a radiation epithelitis with pseudo-membrane formation. The midpelvic dose applied was about 4500 r. with backscatter. The recuperation rate of the normal tissues was about 15 per cent for each treatment following the third fraction and has not been subtracted.

Pathologic Report.—No tumor noted. Much of the tissue now consisted of the fibromuscular layer of the cervix. In places the epithelium was absent, fibrin and neutrophiles forming a thin strip over the denuded tissues. There was considerable hyalinization in the muscle here and an obliterating endarteritis. Where the

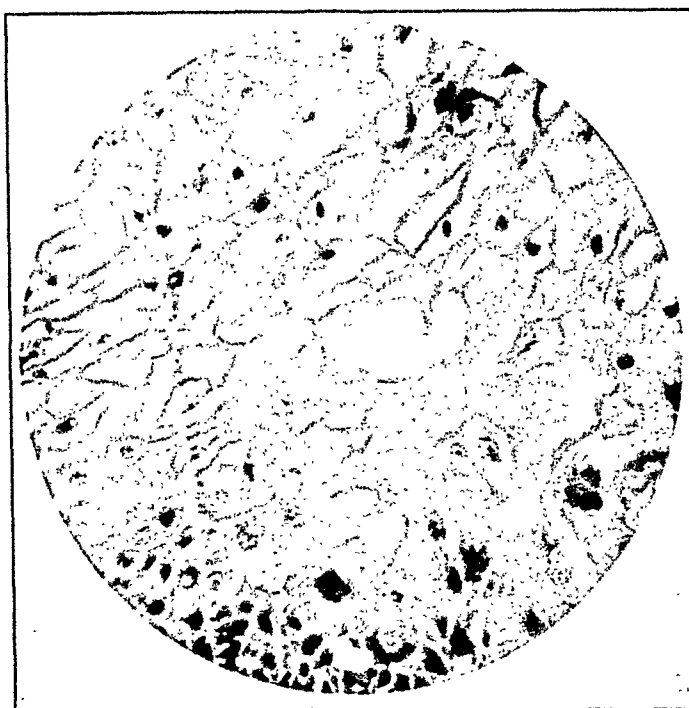


Fig. 4.—Radiation changes after a 2000 r. tumor dose in midpelvis to the now non-cancerous epithelium of cervix. Swelling and vacuolization of cells of prickle cell layer. Nuclei pyknotic or entirely absent. Same magnification.



Fig. 5.—Radiation changes in noncancerous cervical epithelium after 3000 r. had been applied in midpelvis. Desquamation of superficial cells. Minute intraepithelial pustules. "Ballooning" of free end of one cell. Same magnification.



Fig. 8.—Tumor, illustrated in Fig. 7 after intensive irradiation. Magnification same as in Fig. 7. Marked swelling of tumor cells. Nuclei show pyknoses, karyorrhexis and karyolysis. Degenerated pearls with foreign body giant cells in apposition.

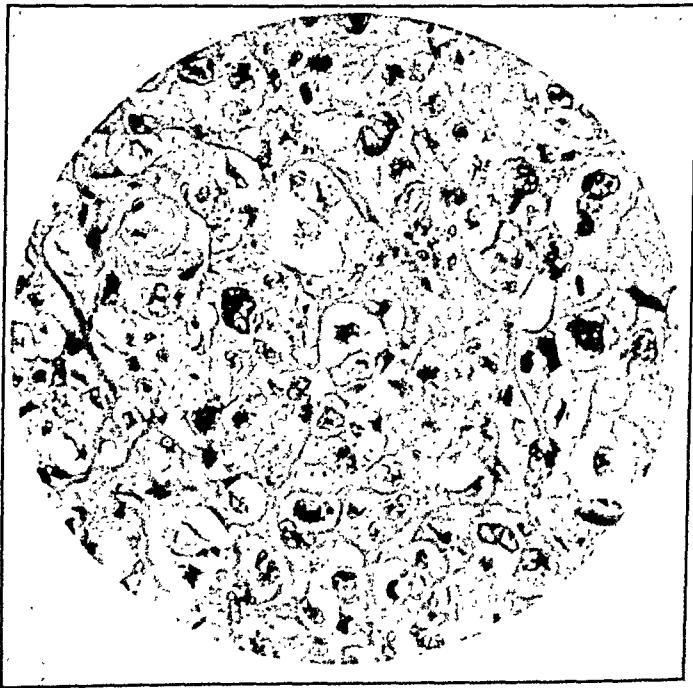


Fig. 9.—Microscopic field adjacent to area shown in Fig. 8. Similar features with exception that giant cells are lacking.

epithelium still persisted, the changes were similar to those described for biopsy 4 (Figs. 4 and 5) but rather more pronounced. In places the epithelial cells had lost their nuclei, staining pale blue, ballooning out from the basement membrane, the superficial layers of the epithelium being absent. Elsewhere there was considerable edema in the lower layers of the epithelium and in the subepithelial tissues. Neutrophilic infiltration here was noted both in the epithelium and in the tissues beneath it.

A biopsy of tissue removed Aug. 9, 1937 consisted of mucus, masses of neutrophils, occasional minute strips of a columnar epithelium, and small fragments of the hyalinized fibromuscular layer of the cervix. No tumor noted.

It is evident that the finding of completely degenerated carcinoma cells albeit a complete absence of tumor cells should not be interpreted as a cure but as an instance of the profound effect of the 800 K.V.



Fig. 7.—Epidermoid carcinoma before intensive irradiation. Squamous cells and pearls depicted. An inadequate radiation had been given elsewhere.

Roentgen rays in a deeply-seated cervix cancer. The steps in the degeneration in a serial number of biopsies may differ, but the slides show decided evidences of an almost generalized degeneration in the tumor mass. Such changes may be seen in simple inflammatory processes, but then they are never as generalized and abundant as in malignant tumors.

Photomicrographs of a radiated epidermoid carcinoma are also introduced here, because of the obviously marked histologic changes shown in them.

The first (see Fig. 7) represents the tumor before intensive radiation therapy. Figs. 8 and 9 are from the same tumor after intensive radiation. The marked swelling of the cytoplasm and nuclei of the tumor cells is well shown. Marked vacuolization of the cytoplasm, karyorrhexis, pyknosis, and disappearance of many

and tanning persisted for another one or two months. The final result is recovery *ad integrum* within about four to six months.

The radiation dermatitis causes burning and itching, and if bleb formation ensues, it causes secretion. The application of pure lard, Dodd's lotion, Edison ointment, and veracol* ointment are used in sequence as the intensity of the changes increases.

Radiation mucositis of the urinary bladder causes frequent and burning urinations which respond to sodium or lithium benzoate. Radiation proctitis produces frequent and watery defecations. A bland diet, the administration of large doses of bismuth subnitrate, resublimed resorcin, sodium or zinc sulfocarbolate and finally pulverized extract of opium are recommended. The radiation vulvitis responds well to applications of zinc ointment.

Latent reactions in the skin or mucosae were not seen if the radiation doses were not increased or repeated. A few instances of intermittent attacks of diarrhea were observed. Persistency in a bland diet would prevent the diarrhea.

THE CHANGES IN THE BLOOD.

The changes in the blood were studied by H. L. Schmitz. The erythrocyte count, hemoglobin percentage, leucocyte and differential counts have been determined routinely before the beginning of treatment and after the fifth, tenth, fourteenth, eighteenth, and twentieth treatments. Significant decreases in the erythrocyte count of 300,000 or more occurred only in ten of 60 cases, and were practically always associated with far-advanced malignant disease. In six instances there was a definite increase in the number of erythrocytes during the course of treatment. The remaining cases showed no significant changes.

Changes in the erythrocyte count were usually but not always accompanied by a corresponding change in the percentage of hemoglobin. In three cases, the hemoglobin percentage fell 10 to 15 points without any decrease in the erythrocyte count.

Changes in the leucocyte count occurred more frequently and were more pronounced than the changes in the erythrocyte count or hemoglobin. The leucocyte count dropped to or below 4,000 in 21 cases. In 19 of these cases, the leucopenia was very transient and the differential counts remained normal. Only two instances of stubborn leucopenia were observed, and these were both associated with multiple metastases to the bones.

RESULTS OF TREATMENT

The 34 primary cases of carcinoma of the uterus were arranged according to the anatomical extent of the growth, namely in four clinical Groups, as used in the Clinic since 1919. Clinical Group I

*Veracol ointment is a 10 per cent mixture of the extract of *aloe vera* in a fatty base.

nuclei are also noted. In addition the epithelial pearls show degeneration changes. Their nuclei disappear and the keratinized remnants act as foreign bodies, foreign body giant cells arising in apposition to them (see Fig. 8). The magnification in all the photomicrographs in this paper is the same: $\times 300$.

These investigations will be continued and the authors hope to report the results at a future time.

Radiation reactions consist of: (1) the constitutional or general reactions termed radiation sickness; (2) the early and late reactions in the skin and accessible mucous membranes of the pelvic organs such as the urinary bladder, the vagina and the rectum lying within the radiation beams; (3) the action on the blood constituents chiefly the red and white blood corpuscles and the hemoglobin; (4) the latent results of treatment on the uterine cancer.

THE SYSTEMIC REACTIONS

The constitutional reactions were negligible with the technique of application of 800 K.V. Roentgen rays evolved in the institute. The patient with an anteroposterior diameter of 24 cm. or less was treated through two fields 15 cm. wide and 20 cm. long over the pubic and sacral regions. The upper limit is the promontory of the sacrum, the lower limit the vulva. Almost 85 per cent of the patients possessed an anteroposterior diameter of 22 cm. or less. The per cent of absorption at a depth of 11 cm. is approximately 50 per cent of that on the surface. This means that the application of a known dose of "r." through two fields produces exactly the same dose of "r." in the center of a pelvis with an anteroposterior diameter of 22 cm. The dose per field applied with 10 equally spaced fractions to each field within twenty-eight days is 4,225 r. Hence the midpelvic dose is 4,225 r. If the anteroposterior diameter is 20 cm., then the midpelvic dose is about 4,640 r., and if it is 18 cm. it is about 5,000 r.

The only untoward symptom was loss of appetite and some nausea which appeared about the time of the twelfth to fourteenth treatments, the same time when the changes in the skin and mucous membranes became marked. Other general constitutional reactions were not observed.

THE LOCAL REACTIONS IN THE SKIN AND MUCOUS MEMBRANES

The early reactions in the skin and mucous membranes exposed to the rays were erythema of the skin and mucosae appearing at the end of fourteen days when about 2,000 r. had been applied; a dry dermatitis and mucositis within twenty-one days, when about 3,000 r. had been given; and desquamation and wet dermatitis and pseudodiphtheritic mucositis at the end of twenty-eight days when about 4,000 to 4,500 r. had been applied. Epilation followed within another week. The entire process showed healing within three weeks but epilation

200 K.V. Roentgen and gamma rays of radium show that the changes in the carcinoma cells occur at much later periods and are never complete, i.e.; they do not show total absence of cancer cells when 200 K.V. Roentgen rays were used.

CONCLUSIONS

A report has been made on the action of 800 K.V. Roentgen rays on (1) the carcinoma cells; (2) the constitution; (3) the skin and mucosae; and (4) the blood constituents.

The changes in the carcinoma cells, i.e., practically complete degeneration and absorption, may occur as early as the midperiod of treatment.

Radiation sickness is hardly ever seen. If it occurs it usually coincides with the time of reactions in the tissues lying within the radiation beams.

The changes in the count of the blood cells and the percentage of hemoglobin are mild and if occurring they are of a transient nature.

The reactions in the skin and mucous membranes lying within the radiation beams are very marked during the last week of the four-week treatment period, but they usually subside very rapidly and completely within four to eight weeks. The skin recovers completely within three to six months.

The three- to four-year arrests of the growth subjectively and anatomically in 34 primary carcinomas was 50 per cent.

DISCUSSION

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—It is recognized that there are three types of cells in carcinomata, the unripe, the midripe, and the ripe. It is not to be understood that the term "ripe," used in the third grouping, refers to normal cells. There is no such thing as a matured carcinoma cell. In all three groups varying percentages of unripe cells are present. Irradiation therapy will have the greatest effect upon the tissue containing the largest majority of unripe cells.

Swelling of the nucleus was noted as one of the results of these treatments, also changes in the chromosomes. It is appropriate to remember in this connection that there are twenty-four pairs of chromosomes in each cell of the human organism and their arrangement so far as is known is in parallel lines. The different types of genes have positions opposite one another. Any disarrangement of this normal placement will interfere with the behavior of the life of the cell or cells.

The mitotic activity of the cells was also discussed. Mitosis will occur in a carcinoma in direct proportion to the size of the cells or in other words, when a certain size is attained division will take place. There is thus a normal relationship between the content of the cell and its circumferential measurement. Disturbance of this relationship is followed by cell division. The use of radium reduces the size of the cells and the number of mitotic changes prevailing.

The presence of pyknotic nuclei denotes that the cells are dead or dying in a great majority of instances. Ten days after treatment it was noted in some sections that no carcinomatous tissue remained. One must face the danger, however, that every worker in this field has recognized, namely, that the penetration of the

comprises the clearly localized beginning carcinoma with a normal mobility of the uterus. Clinical Group II means doubtful localization of the carcinoma within the confines of the cervix, but characterized by a decreased mobility of the uterus. Clinical Group III signifies invasion of one or both parametria but the entire mass is still movable. Clinical Group IV includes the fixed or metastasizing carcinoma. The pelvis is either frozen, or dissemination has taken place to either the bladder, the vagina or the rectum or to distant tissues and organs.

A comparison of the results of treatment was made for different periods in which a different technique was used as seen in Table II.

TABLE II. PRIMARY CARCINOMAS OF UTERUS

A. Treated with 140 K.V.P. R \ddot{o} . and 3000 to 4000 mg. el. hr. Ra from May 1, 1920 to Dec. 31, 1921, showing results of treatment Dec. 31, 1924. Treatments in continuous sittings lasting one week.

Spaced Roentgen Treatment

CLINICAL GROUPS	I	II	III	IV	TOTAL
Number of patients	1	4	10	9	24
Number well	1	2	2	0	5
Percentage well	100.0	50.0	20.0	0.0	20.8

B. Treated with 200 K.V.P. R \ddot{o} . and 4500 mg. el. hr. Ra from May 1, 1926 to Dec. 31, 1927, showing results of treatment Dec. 31, 1930. Treatments spaced and fractioned over three weeks.

Spaced Roentgen and Radium Treatment

CLINICAL GROUPS	I	II	III	IV	TOTAL
Number of patients	5	13	12	18	48
Number well	4	6	2	0	14
Percentage well	80.0	61.5	16.7	0.0	29.2

C. Treated with 800 K.V.P. R \ddot{o} . from May 1, 1933 to Dec. 31, 1934, showing the results of treatment Sept. 30, 1937. Treatments given in 10 equal fractions during four weeks.

Spaced Roentgen Treatment

CLINICAL GROUPS	I	II	III	IV	TOTAL
Number of patients	2	2	13	17	34
Number well	2	2	9	4	17
Percentage well	100.0	100.0	61.5	23.5	50.0

From the results for the Clinical Groups and the periods, it may be stated that the increase in the three- and four-year good end results is due to a marked increase in the percentage of arrested cases in Clinical Groups III and IV. The explanation of this observation may be the more homogeneous distribution of radiation intensities throughout the pelvis obtained by 800 K.V. maximum Roentgen rays in comparison to those by 140 and 200 K.V. maximum Roentgen rays and gamma rays of radium. The microscopic examination of tissues at stated intervals furnishes evidences of the intense influence of the 800 K.V. Roentgen rays on the carcinoma cells. Studies made with

Pain, tenderness, urinary frequency, hip and backache, fever, bowel dysfunction, lower abdominal distress, and low grade of fever are common to both conditions.

The important difference, however, is that in the acute stage of diverticulitis the outstanding symptom of low intestinal obstruction enters the picture, viz., intermittent cramps, the sign of defeated attempts of the bowel to complete a peristaltic wave. As the obstruction progresses, there is of course, a distention of the abdomen within a much shorter time than is the case in acute adnexal disease.

Bimanual pelvic examination elicits the presence of a mass which may be in the right as well as in the left side. There may be pain on movement of the uterus; the latter due to inflammation by contiguity. The process, by extension, may also involve the bladder wall and is the reason for the urinary symptoms. Repeated attacks, when the bladder wall is involved, may end in perforation of that viscus.

An early report of a perforated bladder, the result of diverticulitis, may be found in the publication, "Nine Commentaries Upon Fevers and Two Epistles Concerning Smallpox," addressed to Dr. Mead by, "the late brilliant Dr. John Freind."¹ It was printed in London in 1730. Thus two hundred and seven years ago Freind described in detail, and with excellent follow-up notes, the case of "a very ingenious and studious gentleman who was remarkable for his singular memory. . . ." who was "seized with a pain, flatus, and a sort of convulsion in his bowels." He then, "passed pus and gas per urethram for three months," the author stating that "such a flatus often broke forth with his urine, that the patient seemed to break wind backwards." Autopsy showed an inflamed mass of the colon with a hole into the bladder, "the size of a goose quill."

I believe that this is perhaps the earliest report in English medical literature of this condition, and when one considers the time which has elapsed since then, it does seem strange that a mention of diverticulitis still brings to the mind of many physicians an inflamed Meckel's diverticulum.

The other end-results of a continuation of the disease, with repeated acute exacerbations, may be either perforation of the gut wall, or complete obstruction due to the increasing fibrosis which follows each episode.

The pelvic colon may have diverticula in its terminal portion as well as its beginning. One of these small pockets of peritoneum-covered mucosa, with its bottle-neck-opening into the gut may, because of the irritation of contained infected feces, become adherent to structures in the right side of the pelvis as readily as in the left side. This explains why an attack of diverticulitis may on one occasion cause pain and cramps in the left side of the lower abdomen and pelvis, and at another time, an equally distinct group of symptoms on the right side. Keeping this in mind should clear up some of the confusion which has been continued through the literature in which one finds repeated the statement, that diverticulitis is to be thought of as a left-sided appendicitis.

x-ray or radium varies with prevailing conditions, and the effect upon cells may be reduced as much as 50 per cent for those farthest away from the surface treated.

Another significant factor in irradiation therapy is evident in the tissue reactions. Ordinarily the blood vessel walls become thickened and their lumina will be narrowed. In this group of cases irradiation therapy will be favorable, but in cases where the blood vessels show no reactive ability, irradiation is likely to fail.

DR. JEO VINCENT MEIGS, BOSTON, MASS.—In the *Annals of Surgery* for October is a paper presented before the American Surgical Association in New York in June, showing the results obtained in the Massachusetts Department of Public Health, Pondville Hospital. The results of these cases treated by large doses of Roentgen ray by the 200 K.V. machine plus radium are better than any previous group that has come under my care. The charts of the results are well worth studying.

Our charts show a three-year follow-up to be sufficient to judge a method of treatment, for the deaths after this date follow a perfectly definite curve in all series. Therefore, I am inclined to believe that Dr. Schmitz' cases are going to be almost as good as they are now at the end of five years.

Certainly it is obvious to me that Roentgen ray and radium are better than radium alone. Roentgen ray may supplant even radium.

DR. HENRY SCHMITZ, CHICAGO, ILL.—Without the work of Drs. J. Sheehan and Herbert Schmitz this report could not have been made.

I thank Drs. Davis and Meigs for their kind discussions. The advantage of the x-ray treatment with 800 K.V. lies in the ideal and homogeneous distribution of the radiation intensities throughout the tumor bearing area and the possibility of using much higher radiation doses than with any other kind or quality of rays.

The observations of Dr. Meigs are very valuable. They will enable us to evaluate the advantages of radiation treatment much earlier than the customary five-year periods, and hence predict the correctness of an improved treatment much earlier than usual.

The histologic examinations will be continued. It is evident that the case on the action of x-rays reported today may not be the rule. However, such investigations are valuable to indicate the method of treatment and the radiation doses to be applied to arrest the cancer.

THE DIAGNOSIS AND MANAGEMENT OF DIVERTICULOSIS AND DIVERTICULITIS OF THE PELVIC COLON IN WOMEN*

FREDERICK S. WETHERELL, M.D., SYRACUSE, N. Y.

PELVIC inflammatory disease, either acute or chronic, is not necessarily the result of infections of the female generative tract. The pelvic colon may be the seat of the trouble; yet it is rarely recognized as such until symptoms of obstruction supervene.

Diverticulosis of the colon is not uncommon in the female, and it is important to keep in mind that acute and chronic inflammation of diverticula may resemble in all of their manifestations what we speak of as pelvic inflammatory disease.

*Read at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at Hot Springs, Va., Sept. 20 to 22, 1937.

diet, or even entirely parenteral fluids, is imperative. This regime, even though it is found necessary to continue it for one or two weeks, will in the majority of cases, in a first or second attack, result in a recession of the inflammatory condition and re-establishment of a lumen sufficiently large to permit passage of fecal material. Such treatment will even allow the subsidence of an abscess, and of the markedly inflamed colonic wall.

If, however, nonsubsidence of the abscess is indicated by the usual examination and laboratory findings, something further must be done. Here the pelvic surgeon with his knowledge of pelvic abscesses, due to other conditions, will without doubt advise simple drainage. Whether this drainage is to be by the abdominal route or by a lateral extraperitoneal approach, or as suggested and used by Ralph Weible,⁴ drainage through the anterior wall of the rectum, will of course depend on the location of the mass and the experience of the surgeon. In these cases however, vaginal drainage is contraindicated because of the possibility of fecal fistulas following such drainage. The rectal approach seems to be the most logical one, providing, of course, that the abscess is in a position to be reached.

The next order of procedure is aimed at establishment of abscess drainage and decompression of the bowel. When colostomy is contemplated, the fundamentals of good abdominal surgery indicate that the farther away from the acute inflammatory condition, the better for the patient. Therefore, a cecostomy of the type which will insure nonclosure of the stoma is the procedure of choice. I would here reiterate, that complete low obstruction may be tolerated for ten days to two weeks and that these patients quiet down as a rule, and not as an exception. Therefore, any form of colostomy is to be put off as long as possible.

Involvement of the bladder wall with its coincident irritation and urinary dysfunction, and perforation into that viscus are problems, the solution of which need not be detailed to those familiar with pelvic surgery. Suffice it to say that in the event of such perforation, it would without question be advisable to decompress the bowel by cecostomy, evacuate abscesses by drainage, and wait for a complete quiescence of the disease before attempts at repair are instituted.

The literature of the past two years indicates that the error of attempting a colostomy just proximal to the inflamed area at the same stage in which drainage is done, is still being made. One such error occurred in a case which I saw in consultation with the surgical department of one of our hospitals. I was called in to determine the possibility of the presence of a pathologic condition in the pelvis.

A diagnosis of acute diverticulitis with abscess was made and drainage advised. The patient was operated upon by a member of the surgical division and a colostomy done, with the drainage operation. The woman survived forty-eight hours.

Most authors speak of the difficulty of palpating a mass, but if one familiarizes oneself with the feel of the normal colon, by abdominal palpation, it is not difficult to notice a change in size when this viscus is distended, or, as occurs in diverticulitis, distended and hardened by the inflammatory reaction surrounding it. This palpation is best done by using one hand for sensation and the other, superimposed upon it, for purposes of pressure.

INCIDENCE

Last year, Rosecoe R. Graham of Toronto,² made a study of the incidence of diverticulitis in 44 personally observed cases. He found that "such diverticula are present without symptoms or any clinical evidence of their presence in approximately 5 per cent of persons subjected to a routine x-ray examination of the colon for any cause. Of this 5 per cent, approximately 12 to 15 per cent develop diverticulitis. To translate this into the incidence occurring in a family practice, we grant that 1,000 patients constitute a practice; we grant that 250 will be over forty years of age; 12 of these will have diverticulosis, and at least 1 will have diverticulitis. . . . When one considers that in a family practice there is on the average only one case of duodenal ulcer under active treatment, we realize that from the general practitioner's viewpoint, his problem with sigmoid diverticulitis should be as great as with duodenal ulcer, and yet the interest and discussion of these two disease processes show a great disparity."

This study, I am certain, is correct in its conclusions. Furthermore, one finds in the literature of the past three years figures which indicate that women make up from 30 to 45 per cent of the number of cases of diverticulosis and diverticulitis. It is my feeling that an alertness on our part will uncover many more cases of both the chronic and subacute types of the disease in women who come for treatment because of low abdominal or pelvic distress.

MANAGEMENT OF THE ACUTE CONDITION

As Thomas E. Jones, of Cleveland,³ said before the American Proctologic Society at Kansas City, Missouri, in May of 1936, "It is easy to tell the other fellow what to do with his cases, but when it comes to advise your own, it is not so easy." Nevertheless, we have three fundamental conditions or complications with which to deal in the acute exacerbation of a diverticulosis. They are: (1) A low obstruction of the colon. (2) Perforation with infection and abscess formation behind the sigmoid flexure of the colon, or, rarely, into the peritoneal cavity. (3) Inflammation of the bladder wall by contiguity which if long continued may end in perforation and drainage into the bladder.

In dealing with the first of these conditions, we must keep foremost in our minds the fact that an obstruction in the terminal colon, sometimes quite close to the rectum, is not of the same serious import that a higher obstruction is, particularly one in the small intestine. As a rule, the obstruction is preceded, for several days, by a gradually increasing partial-obstruction of the lumen, with cramps, followed by the expulsion of gas and either solid or liquid feces. With this picture in mind, it can be seen that complete bed rest, preferably in a hospital, with a liquid

examination, and it should be done by the contrast method, in which the lower colon is inflated with air, following the expulsion of a barium enema, will reveal in the majority of cases the existence of the disease.

X-ray examination is definitely contraindicated during the acute stage.

Having discovered the presence of a diverticulosis, it is then our duty to make clear to the patient the future which confronts her unless the greatest care in following a dietary regime is exercised, and the other routine mentioned elsewhere, is meticulously carried out. So often do acute attacks occur following mild upper respiratory infections, and subsequent to overtiring activities, especially heavy lifting, that it is well to impress such dangers upon the patient. There is nearly always a tendency to obesity in these individuals and for that reason, the diet, in addition to being relatively "residue-free," should also be regulated in regard to keeping the weight down.



Fig. 1.—Sigmoid colon shows numerous diverticula, one particularly large one extending to the right side of the pelvis. (Mrs. R. Aged 58 years.)

The discovery of the presence of the disease by a careful inquiry into the patient's history regarding episodes of bowel dysfunction accompanied by low abdominal and pelvic distress, is, if anything, more important than management of the acute stage. Only by so doing will we be able to warn of the dangers and so help these individuals to avoid the acute attacks which are always imminent. Both gynecologists and abdominal surgeons have here a much neglected field.

Two short case histories illustrate this point:

Mrs. R., fifty-eight years of age, was operated upon for relief of a descent of the uterus April 25, 1936. In her history appeared the following: Bowels always fairly regular with some tendency to constipation. About four years ago, the patient was taken with pain in the left lower quadrant of the abdomen. This pain was fairly severe and lasted several days. It was cramp-like in character and was accompanied with nausea and vomiting, and diarrhea. Since that time she has had three other at-

The management of this condition will parallel that of acute salpingitis which, in the early days, was accompanied by a high death rate because of ill-advised abdominal sections. These patients are too sick for any extensive procedure, and for that reason, drainage alone should be resorted to, for, in the event that this does not suffice, no harm has been done, whereas an added colostomy (except perhaps cecostomy) adds from 50 to 75 per cent to the mortality rate.

MANAGEMENT

Acute Stage.—It must be remembered that the obstruction is low, sometimes quite close to the rectum, and that such a location permits of long bowel stasis without imminent danger. The patient should be either on parenteral or liquid nourishment. A few days to two weeks may be long enough for the acute process to subside following simple drainage of the abscess, and thus a patent lumen becomes established through the mass. This has been my actual repeated experience and is the foundation for my belief that drainage alone should be resorted to as a relieving measure for abscess, and that even drainage is to be avoided until the general signs of abscess, and lack of abatement of the obstruction, indicate that something *must* be done. Bowel function may be established without surgical interference even after a week to ten days of complete low obstruction, provided of course that there is evidence of subsidence of an acute inflammatory process.

If colostomy must be resorted to, it is perhaps best that a permanent type of opening be made with invagination and closure of the distal segment. Present-day management of such a stoma has eliminated the old bugbear of colostomy. However, the fact that proper management of the diverticulosis following an acute attack offers the patient a comparatively comfortable and long life, argues for the utmost in conservatism during an acute attack.

Bowel resection, when the disease is low in the pelvic colon, is attended by such technical difficulties, and such high mortality rate, that it is fair to say that it should never be attempted.

Quiescent Stage.—Once an acute attack, always the likelihood of another. It is sufficient to say that a relatively residue free diet with elimination of gas forming starches (particularly potato), and condiments, plus the avoidance of emotional disturbances, which initiate an increased intestinal peristalsis, and heavy lifting which results in increased intra-abdominal pressure, are the general rules which the patient must follow if the danger of acute exacerbation is to be avoided.

Subacute Stage.—This condition has been almost entirely overlooked by writers. A low-grade inflammatory process may continue over a period of weeks or even months and is the cause of intermittent low abdominal and pelvic distress. It is during this stage of the disease that women often seek the advice of the physician. The symptoms are those attendant upon any pelvic inflammation plus evidences of bowel disturbance. There is a general low abdominal soreness, and to be particularly noticed is the distress which accompanies walking, or being jarred while in a sitting position. The latter, of course, occurs during automobile rides or train journeys. The patient feels as if she were carrying around a sore mass which must be treated with a great deal of gentleness. She bends forward when she walks and is likely to support her abdomen with both hands to relieve the feeling of pressure and to save jarring. Bearing down during defecation is a painful procedure and the same holds true during urination.

This train of symptoms should make one suspicious of the existence of the condition, and it is at this time when examination by x-ray is indicated. Such

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—It has been my experience twice this year to subject the pelvis to surgical exploration for what I thought was an ovarian tumor, but what proved to be diverticulitis which had become adherent to the left adnexa. Why is such a mistake made? First of all, in a pelvis in which diverticulitis is present the inflammatory process is as a rule higher up than it is when adnexal disease alone is present. Usually, the mass is more or less mobile. The best diagnostic procedure is to place one finger in the vagina and the other in the rectum and determine if you can move the rectal wall separately from the adnexal mass. Suppose the abdomen has been opened and this condition has been encountered, what should one do? If the mass is only very lightly attached to the adnexa and can be separated easily, it is best to mobilize the mass, wrap the lesion with the omentum and bring it over to the midline of the pelvis. The abdomen should then be closed as it is after an exploratory laparotomy and conservative medical treatment should be employed.

If the lesion is extensive and a tuboovarian inflammation is present, should one proceed with the primary radical operation? I do not think this is advisable as the risk is too great. Therefore, one should divert the fecal stream by a colonic stoma in the descending colon well above the lesion and should forget about it for two or three months and decide later what should be done. Perhaps nature will take care of the whole condition and one will need to do nothing else but close the colonic stoma.

One must always keep in mind that diverticulitis is an important disease, and in operating in the pelvis of women, it is well to examine the sigmoid colon and see if there are any diverticuli, because it has been my experience to find some which have exudate around them and which are totally unrelated to any other pelvic condition. If one fails to recognize them and they are injured, the patient is liable to die of peritonitis, as often happens in cases of infected carcinoma or ulcerative colitis. By merely touching the areas that are inflamed, the organisms go right through the intestinal wall and produce fatal peritonitis.

I was very much interested in Dr. Wetherell's findings because they coincide almost identically with those of my colleague, Dr. P. W. Brown. It has been shown that 5 or 6 per cent of all people have diverticulosis. The ratio of diverticulitis to diverticulosis is 1:6 or 8. Operation was done in 68 per cent of the cases. The situation of the lesion was usually in the sigmoid colon. Proctoscopic examination will reveal the extent of healthy intestine distal to the lesion. If it is necessary to do a resection, one must know what healthy bowel is available for anastomosis. Bleeding from diverticulitis is not common. If there is bleeding, carcinoma must be suspected because diverticulitis is not a mucosal lesion.

Dr. Wetherell spoke of obstruction. These patients do have obstruction, but we found in this group that the obstruction was not the outstanding feature. Patients usually referred to pain and had fever and leucocytosis. In 18 cases there was a fistula into the bladder; in 12 of the 18 cases obstructive phenomena were not present. There is no particular relationship between diverticulitis and carcinoma.

Of the 99 patients that were subjected to operation, 46 were benefited, 16 died immediately or within a few months after operation, and 19 continued to have trouble. We have tried medical treatment at the clinic but in most of these cases the complications demanded operation either because of abscess or perforation. The patients who do not have complications are treated medically and get along well.

With regard to medical treatment there are one or two points to be emphasized. Heat has been used within the last year where abscess has developed. We found that by introducing heat into the rectum, either by the Elliott principle, by two-way irrigation of the rectum with hot oil or hot water, or by diathermy, after about ten or

attacks, two years ago, one year ago, and about six weeks ago. During the last attack there was pain but no diarrhea, nausea, or vomiting. She has never had any bright red blood passed from rectum or had any tarry stools. Pain was quite severe and there was some bloating of the lower abdomen. For several days soreness followed the pain. These were the only changes in bowel habit, and when well there had been no change in the type of stool. At times she notices some mucus.

Because of these findings an x-ray examination was ordered and the diagnosis of diverticulosis was confirmed (Fig. 1). This woman has not had any attacks since operation and is carefully following regime.

Mrs. C., aged sixty-four. This woman's history disclosed the fact that she had had a feeling of fullness in the lower abdomen and often became distended with gas. She felt as if there was "a place where gas had difficulty in passing, low down." After the gas passed this point and entered the rectum, she was relieved. A diagnosis of diverticulosis was confirmed by x-ray studies. The picture is so much like that in Fig. 1 that it is not reproduced here.

Her operation, done on Feb. 25, 1936, was also one for descensus uteri. She has had no attacks since following a proper regime of bowel management.

SUMMARY

Diverticulitis of the pelvic colon in women has many of the earmarks of so-called pelvic inflammatory disease.

Obstructive symptoms, during an acute attack, plus a history of previous bowel disturbances accompanied by cramps, are the important differential diagnostic points.

Management of the acute stage should lean toward conservatism. Operative interference is not as essential in low colonic obstruction as elsewhere in the intestinal tract.

Careful inquiry into the history of bowel disturbances which are accompanied by low abdominal and pelvic distress, checked by x-ray examination, points the way to prevention of acute attacks. A "residue-free" diet, and a gentle mode of living are the essentials of prophylaxis.

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713 EAST GENESEE STREET

DISCUSSION

DR. E. A. VANDER VEER, ALBANY, N. Y.—It was not so many years ago that we grouped practically all the pathology in the female pelvis due to infection under the generic term pelvic inflammatory disease, and considered that 80 per cent of the cases were due to a specific infection. Our present knowledge of the pathology of the female pelvis shows us that that supposition was wrong and that many factors enter into the causation of the pelvic inflammatory disease. As I look back now over some of my pelvic cases in which the apparent cause of the inflammation was obscure, I have no doubt that the pathology was caused by diverticulitis which I failed to recognize.

A STUDY OF CERTAIN DIETARY FACTORS OF POSSIBLE ETIOLOGIC SIGNIFICANCE IN TOXEMIAS OF PREGNANCY*

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DURING the past few years there has been a healthy "opening up" of the so-called toxemia of late pregnancy. In a most comprehensive paper Kellogg¹ has summarized the different thoughts. The suggestion again has been made that the term "toxemia" be discarded; since no one has ever demonstrated a toxin, many have favored this change. However, Dr. Lee thought this term should be retained until the correct term is forthcoming. The classification is being altered and new factors are being investigated and old ones reevaluated. Peters² and others have recalled the association of urinary infection. Irving and others³ studied and evaluated the vascular phenomena.

In order to add to the sum total of information regarding these conditions without adding to the confusion, all pertinent data should be recorded and be subjected to comparison and to checking. The only single factor that is consistent is the state of pregnancy. The variables of severity, mortality, and other manifestations in different localities and years have been recorded. We have not been able to report such favorable figures as Rucker,⁴ Siebel,⁵ and Colvin⁶ in neighboring states. We have found urinary infection and essential hypertension in the private patient group more often than in the lower stratum where we have found eclampsia. That eclampsia and puerperal albuminuria have been the most frequent and the most severe obstetric complications in North Carolina is best shown by the tables which are given later.

Bland⁷ in analyzing various reports quoted an incidence of toxemia of pregnancy of 13.5 per cent as the cause of death in 153,598 maternal deaths in this country from 1921 to 1928. In Great Britain the incidence from this cause was 19.8 in 1596 maternal deaths.

In the final report of the Commission on Medical Education the cause of death from toxemia was 27 per cent. This was a study of the years 1926 to 1928 when the maternal death rate was 67 per 10,000 live births. In the maternal mortality in 15 states* 7,537 maternal deaths were studied and the rate was 64 deaths per 10,000

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twelve treatments the mass will be tremendously reduced. If operation is then considered advisable, it can be done with less risk and better chance for successful result.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—One doctor, who had suffered from the disease for about twenty years, told me that he was relatively comfortable on what he termed a "cow" diet. Instead of foods with seeds and fine cellulose particles, he partook freely of leafy vegetables with long fibers, which held the fecal masses together so that they slid over the openings of the diverticuli and at the same time overcame the tendency to constipation. Many of these patients seem to be relieved to a degree by bismuth or barium, carried to the pouches by enemas.

A chronic type of perforation often occurs without an acute attack. While apparently in his usual health, the patient may suddenly note the presence of gas and fecal matter mixed with the urine, or a mass developing in the left groin, or material from the ileum mixed with feces. The colon infection from a fistula into the bladder is serious, and if it continues for any considerable time, it may lead to a permanent or even fatal infection of the urinary tract.

As for colostomy, the simplest type is to pull the appendix and the mesoappendix through a muscle splitting incision one or two inches long. Dressings are applied, the tip of the appendix then cut off and a small catheter introduced. No sutures are required. Daily a larger catheter is substituted and at the end of a week we have had a rectal tube size 27 or 28 cm. into the rectum. But the appendix in elderly persons is often atrophic and too small, when the side of the cecum is utilized. The mass of diseased bowel from a diverticulitis can usually be removed with greatest safety by a Mikulicz type of operation.

DR. JAMES W. KENNEDY, PHILADELPHIA, PA.—I would like to ask Dr. Wetherell about the right-sided pain. How many of the patients had pain in the sigmoid region?

DR. WETHERELL (closing).—The anatomic layout of the pelvic colon takes it to the right side of the pelvis and then back in the form of an "S." This is the reason for the term, sigmoid. If our diagrams of the pelvic colon were made to depict this "S," it might clear up much of the confusion concerning right-sided pain due to pelvic colonic disease.

These patients have a definite history which of course must be obtained. They are sometimes severely ill for a few days and then suddenly feel much better. The cramps during the attack are severe enough to necessitate confinement to the house. Every time the bowel begins to contract and by its peristaltic action tries to force something through the inflamed, narrowed lumen, there is a cramp. Having had such an attack for several days, and then suddenly having the pain quiet down, makes the patient anxious to forget that upset. The patient may not tell about these attacks unless careful inquiry is made into the history of bowel disturbances.

I have tried to stress the point that you can wait with a low obstruction. Bowel movement is not necessary for ten days or two weeks.

So far as doing a Mikulicz operation on a rectosigmoid mass, particularly where there is a diverticulitis, I must disagree with Dr. Babcock. It has a high mortality.

TABLE III

NEW YORK STATE 1932		NORTH CAROLINA 1933	
KOSMAK		HAMILTON	
285 DEATHS		268 DEATHS	
30%	Sepsis	19%	
24%	Hemorrhage	13%	
23%	Toxemia	43%	

saw their physician and that only 17.6 per cent reported for examination when they were presumably well. "If we assume that adequate prenatal care must begin before the end of the fourth month of pregnancy, only 74 of the 1,396 having answered this question gave their physician a fair chance to give them protection. This constitutes only 5.2 per cent of the total. In the second report approximately 9 per cent of the small number included in that study reported to the physician before the end of the fourth month. It is evident that we have not yet made progress in our efforts to provide adequate prenatal care to those of our citizens who are creating new life."

In previous papers^{13, 14} we have given our statistics, and emphasized the similarities and differences between our series of late toxemias, drawn largely from rural North Carolina, and those of other investigators. Lately our attention has been focused on certain characteristics which seem fairly constant. We have been struck with the number of patients with eclampsia who have been in a very poor state of nutrition. They have not been so often the plethoric, stout individuals that fulfill the classic description of the eclamptic type. On checking the localities from which they have been referred and on reviewing the state morbidity and mortality statistics, we have found that in the same areas in which eclampsia occurred most often we were likely to find a large percentage of pellagra and similar diseases. On close and repeated questioning and investigation, we found that the patient that we see in eclamptic convulsions has come from the same group who subsisted on a pellagra-producing diet. Ruffin and Smith¹⁵ have written in detail on pellagra and deficiency diseases in this state. Table IV gives the death rate from pellagra in women in childbearing age in North Carolina.

TABLE IV. DEATHS FROM PELLAGRA IN WOMEN OF CHILDBEARING AGE

1931	275	1934	155
1932	167	1935	174
1933	150	1936	165

These figures (Table IV) are quite similar to the late toxemia deaths. The analogy approaches even more closely when the diet is analyzed in more detail (Table V).

Thus we see that the diet is grossly deficient in all the vitamins especially A, C, and D, as well as being inadequate in the minerals. The energy producing elements are adequate as a whole but there is

live births. Puerperal albuminuria and convulsions were the cause of death of 1,900 women or 26 per cent. The majority of these patients were from the rural districts and the incidence among the colored race was relatively higher. The Maternal Mortality Commission in New York City⁹ reviewed the cause of death in 2,041 patients and found toxemia as the cause in 230 patients or 14.8 per cent, and this was greatest in the fifteen- to nineteen-year group (24.1 per cent). The maternal mortality in the Philadelphia¹⁰ report listed toxemia as the third largest cause of death. There were 7,700 deaths and 114 were due to puerperal albuminuria and eclampsia (15.8 per cent). In North Carolina puerperal albuminuria and eclampsia have accounted for 25 to 35 per cent of the maternal deaths.

The population of North Carolina in 1930 was 3,417,000, of which 35 per cent was colored and 70 per cent was rural. The live birth rate was about 25 per 1,000 population or about 75,000 a year. The stillbirth rate was 40 per 1,000 live births. The general death rate was about 33,000 to 34,000 a year.

TABLE I

	NO. MATERNAL DEATHS	NO. BIRTHS	RATE	ALBUMINURIA AND ECLAMPSIA	
1932	555	77,880	7.1	185	33.3%
1933	535	75,322	7.1	175	32.7%
1934	605	79,556	7.6	181	29.9%
1935	554	79,596	7.0	147	26.5%
1936*	497	76,869	6.5	135	29.7%
	<u>2,746</u>	<u>389,223</u>	<u>7.1</u>		

*Provisional.

The local problem is graphically detailed by Bradford¹¹ who is quoted: "It is my belief that in the three states of North Carolina, South Carolina, and Virginia the relative importance of the contributing cause of maternal mortality cannot be compared with metropolitan centers for the factor of lack of proper prenatal care is a greater problem in our rural communities than in the urban areas." In 1932 in the State of North Carolina 26,077 women (33 per cent of birth registrations) were delivered by midwives. In New York City 8.5 per cent of pregnant women are delivered by midwives. An interesting table (Table II) shows the contrast.

The comparison with a like number of patients in another state is recorded.

TABLE II

12,041 DEATHS. NEW YORK CITY. (COMMONWEALTH FUND)		334 DEATHS. NORTH CAROLINA. (STATE BOARD HEALTH)	
17.5%	Abortion	11%	
25.0%	Sepsis	15%	
9.7%	Hemorrhage	10%	
12.0%	Toxemia	41%	

Hamilton¹² has classified the maternal deaths as related to the time of pregnancy that the pregnant woman first consulted a doctor and found that 82.4 per cent of the total had some complication of pregnancy or concurrent disease when they first

We have analyzed in some detail the progress of patients who have been delivered at the maternity home. These patients came from the rural districts and as a rule were single and arrived at the hospital in a very poor state of nutrition, due to the worry of being pregnant, poor home conditions, not eating in the hope of not gaining weight, and not having received medical attention. The home was operating on a very small budget and had difficulty in supplying the actual food and accessory factors that could improve and overcome this condition. An analysis of 200 cases from 1931 to 1933 records showed an astounding incidence of toxemia. Thirty cases developed symptoms and signs of toxemia, viz., headache, epigastric pain, edema, scotomata, general malaise associated with a rise in diastolic blood pressure above 90, a rise in systolic pressure above 140 and albuminuria, and of these 16 cases showed moderate to marked pitting edema, elevation of blood pressure and albuminuria and fell definitely into a preeclamptic group. Five patients had eclampsia, 4 had severe generalized convulsions before delivery, and 1 developed convulsions twenty-four hours following delivery.

Since many of the cases had been under observation for three to four months and since 28 of the 30 patients with toxemia showed progression of symptoms during their stay at the hospital, an opportunity was offered to study the environment conducive or contributing to this disorder.

Blood studies observed over periods of twelve weeks showed moderate to severe secondary (microcytic) anemia in 21 per cent of the cases. The initial determination of red blood cells in these cases showed a variation in red blood cells from 2,090,000 to 3,970,000 with an average of 3,400,000. Since there had been no history of blood loss, and since the diet in all cases had been questionably to definitely deficient in iron containing foods and the anemias were more severe than the physiologic anemia of pregnancy, they were thought to be nutritional. With improvement in the general economic conditions, helpful suggestions as to the diet and added personnel there has been a decrease in the incidence of toxemia. The institution's diet is now considered adequate remembering that the prophylactic dose of the vitamins and accessory factors is less than the curative.¹⁸

This series of experiments was performed in order to compare the effects of an ordinarily adequate diet with those of a questionably adequate diet upon the incidence of toxemias of pregnancy in a group of young women. The uniformity of the group lay in the parity, in the age range (sixteen to twenty-two), origin in about the same lower economic and social stratum of society, and an absolutely uniform environment during the period of our study within the confines of a small charitable institution.

a protein deficiency. The animal protein consists chiefly of pork which varies with the season. It is over abundant in the Fall and Winter but inadequate in the Summer. With no sharp demarcation there are three dietary groups of patients in North Carolina: the intelligent economically capable, the fairly cooperative adequately nourished, and the uninformed improperly nourished medically inarticulate group. We have rarely found toxemia in the first two, but it is the prime factor in maternal mortality in the last. We suggest that the incidence of the malnourished pregnant women who do not seek medical attention and who develop late toxemia and of those with deficiency disease may simply be parallel.

TABLE V

ARTICLE	QUAN- TITY (GM.)	PRO- TEIN (GM.)	CARBO- HYDRATE (GM.)	FAT (GM.)	MINERALS (GRAMS)			VITAMINS				
					CA	P	FE	A	B	C	D	G
Corn meal	92	8.3	69.0	2.0	0.011	0.1225	0.0006	+				±
Cane syrup	105		89.2					+				+
Flour	111	12.5	83.4	1.2	0.022	0.1030	0.0010	+				-
Lard	81			81.0				-				-
Rice	25	2.0	19.6	0.1	0.0023	0.0240	0.0002	-				-
Field peas	90	19.2	54.6	1.4	0.0756	0.0760	0.0052	+	++			+
Hominy grits	51	4.3	40.6	0.3	0.0056	0.0734	0.0005	+				-
Fat salt pork	60	1.1	0.0	51.3	0.0011	0.0115	0.0001	-				-
Calories	2890.0											

Adequate and regulative diet is of prime importance in both groups. Urinalysis, blood pressure, and weight recording and various blood estimates are informative. We feel that even though we should carry out a most comprehensive antenatal routine (Irving¹⁶) and not be able to arrange and supplement the diets of the patients described, we would probably find symptoms of late toxemia of pregnancy developing in a greater proportion among this class of patients. However, Theobald¹⁷ in three years saw only 7 or 8 cases of eclampsia, while in charge of the largest obstetric service in Siam, yet all types of infections especially urinary infection were present in the pregnant patients. The diet was deficient in vitamins A and B. His observations of the habits of women in Siam are most enlightening.

We wrote to our confreres in five widely divergent localities within the State and found that there were 44 toxemic deaths in one year. These counties had a total of 77 deaths from pellagra 35 of which were in women in the childbearing age.

We have investigated our hospital records (Watts, Salvation Army and Duke) for four years and found that 160 females have been treated for pellagra. Only seven of them were pregnant and one of the seven had symptoms of late toxemia. One patient had sprue. During the same period of time there were 2,120 patients delivered in these hospitals and 154 patients with late toxemia of pregnancy. Our mortality rate for this complication was about 13 per cent.

LIST I

Frances: Poor appetite. Self-restricted diet.

Breakfast 1/4/37

2 slices bread
1 slice butter
1 cup coffee
1 cup milk
1 apple

Lunch

1 bowl soup
1 slice bread

Supper

3 slices French toast
1 slice butter
syrup

Breakfast 1/5/37

1 egg
 $\frac{1}{2}$ cup coffee
 $\frac{1}{2}$ slice butter
1 glass milk

Lunch

1 serving meat
2 slices bread

Supper

2 slices bread
1 slice butter
1 slice bologna
1 glass milk
1 choc. pudding

Breakfast 1/6/37

1 slice bread
1 apple
1 glass milk
 $\frac{1}{2}$ cup coffee

Lunch

1 piece bread
1 small potato
1 small serving gravy

Supper

1 glass milk
1 serving potatoes
1 dessert (apple sauce)
1 slice bread and butter

Breakfast 1/7/37

1 glass milk
1 egg

Lunch

1 serving slaw
1 serving macaroni
1 serving tomatoes
1 potato

Supper

1 serving corn pudding
1 roll
1 slice butter
1 dessert (pears and cake)

Breakfast 1/8/37

$\frac{1}{2}$ grapefruit
 $\frac{1}{2}$ roll
 $\frac{1}{2}$ cup coffee
1 glass milk

Lunch

1 potato
1 slice meat

Supper

1 bowl beans
 $\frac{1}{2}$ slice bologna
2 slices bread
1 slice butter
1 dessert
1 glass milk

Breakfast 1/9/37

1 apple
1 glass milk
1 cup coffee

Lunch

1 serving rice
1 serving peas
1 serving gravy
1 serving meat
3 slices bread

Supper

1 serving peas
1 serving tomatoes
1 serving jam
1 slice butter
5 biscuits
1 glass milk

Breakfast 1/10/37

1 egg
 $\frac{1}{2}$ slice butter
 $\frac{1}{2}$ grapefruit
1 cup coffee

Dinner

2 serving peas
1 serving
pickles
potato chips

Emphasis was recently laid by Strauss¹⁹ upon the possible rôle played by the protein intake and the level of the plasma proteins in the development of water retention as one of the important manifestations of toxemias of pregnancy. By feeding 15 women with toxemia of pregnancy, a very high protein diet (260 gm.) supplemented by parenteral administration of liver extract as a source of vitamin B complex, Strauss was able to induce in all three patients loss of weight attributable to a loss of edema together with a disappearance of symptoms of toxemia.

Since a diet containing 260 gm. of animal protein (meat, fish, eggs, milk) was both economically and physically impracticable, especially in the lower economic strata of the population, we attempted to render a diet which (1) was barely adequate in regard to protein, vitamins, and minerals, (2) liberally adequate in these respects and yet keeping it within the limits of availability to even moderately poor families. With this purpose in view the regular diet of the institution was taken as basic or control for this group of patients.

The 56 patients in this study received the regular diet of the institution under the supervision of a competent matron and of a nurse. This diet, a record of which was kept in a daily menu sheet, represented that common to charitable institutions maintained on a very limited budget. There was an abundance of the cheaper items, such as bread and cereals, but great restriction in regard to the more expensive items such as fresh fruit, milk, butter, eggs, meat, and fish products. During the winter season fresh vegetables are also limited. It is to be noted that the attitude of the staff toward the patients was a highly benevolent and kindly one, and the patients were permitted to eat all they wanted of the foods that were abundantly available, chiefly bread, cereals, potatoes, and some vegetables. This is illustrated in the dietary for one week for two patients given in Lists I and II. These were chosen as illustrative in a contrasting way of the intake of food of a patient with a good healthy appetite and of one with a poor appetite. An estimate of the average daily intake in terms of grams of protein, fat, and carbohydrate and of the caloric values is also indicated. Allowing for individual variations in appetite, the consumption was 35 to 70 gm. protein, 46 to 106 gm. fat, 102 to 266 gm. carbohydrate, and 964 to 2080 calories.

As far as the caloric intake goes it was obviously more than ample to take care of the actual needs of these women all of whom were inactive, even after taking into account the increased basal metabolism in the last months of pregnancy (summarized by A. W. Rowe²⁰). The adequacy of this diet in regard to proteins, minerals, and vitamins, was less certain. According to Sherman²¹ "There seems to be little if any need for increasing the ordinary intake of protein during

Lunch

- 1 serving beans
- 1 serving potatoes
- 1 serving turkey
- 1 serving dressing
- gravy
- celery
- 4 slices bread

Supper

- 1 bowl beans
- 1½ slice butter
- 3 slices bread
- 1 glass milk
- 1 dessert

Breakfast 12/28/36

- 1 bowl oatmeal
- milk and sugar
- 3 slices bread
- 1 slice butter
- 2 cups coffee
- milk and sugar
- 1 apple
- candy

Lunch

- 1 large serving turkey pie
- 1 serving snap beans
- 1 serving gravy
- 3 servings peas
- 5 slices bread
- candy

Supper

- 1 bowl turkey soup
- 1 serving Irish potatoes
- 1 serving chicken salad
- 3 rolls
- 1 slice butter
- 1 small serving jelly
- 1 slice cake
- candy and nuts

Breakfast 12/29/36

- 1 bowl cornflakes with
- milk and sugar
- 2 rolls
- 1 slice butter
- 1 egg
- 2 cups coffee
- milk and sugar

Lunch

- 1 serving cabbage
- 1 serving beans
- 1 serving potatoes
- 1 serving meat
- gravy
- 3 rolls

Supper

- 1 bowl beans
- 2 slices bologna
- 2½ rolls
- 1 slice butter
- peach preserves
- 1 glass milk
- 1 dessert (pears with cake)

pregnancy and some reason for caution in doing so. The surplus over actual need which most ordinary dietaries contain seems ample for the needs of pregnancy." (On the other hand Sherman, i.e., 464, quotes Smith (*Lancet* 2: 54, 1916) to the effect that "maternity hospital records have shown that women classified as under-nourished during pregnancy showed greatly increased proportions of stillbirths, of premature births and of deaths of babies within ten days after birth."

It should be noted, however, that by far the largest proportion, estimated as 70 per cent, of the protein was furnished by the cereals and only approximately 30 per cent by meats, milk and eggs. It is conceivable that, while the total amount of protein was adequate, the quality of the protein, or the quantity of the type of protein best suited for replacement of maternal tissue and blood proteins was not entirely adequate. This possibility was borne out by the discovery of the relatively low plasma protein values shown in the charts and discussed later. Also on the basis of our knowledge of the group of the population from which most of the subjects came, the dietary before admission to the hospital of these patients was very likely to have been deficient both in the quantitative and qualitative aspects.

LIST II

DIETS SALVATION ARMY HOSPITAL

Irene: Liberal diet, good appetite.

Breakfast 12/22/36

- 1 bowl cornflakes
- 2 rolls
- 1 egg
- 1½ slice butter
- 2 cups coffee

Lunch

- 1 serving rutabagas
- 1 serving string beans
- 1 serving sweet potatoes
- 1 serving gravy
- 1 slice meat
- 3½ rolls

Supper

- 1 bowl peas
- 3 slices bread
- 2 slices butter
- 1 serving potatoes
- 1 dessert
- 1 glass milk

Breakfast 12/23/36

- 3 slices of bread
- 1 slice of butter
- 1 bowl of cream of wheat
milk and sugar
- 1 orange
- 2 cups of coffee

Lunch

- 3 slices of bread
- 1 serving of peas
- 1 serving of potatoes and gravy
- 1 slice of meat

Supper

- 1 bowl beans
- 1 slice bologna
- 3 slices of bread
- 1 slice of butter
- 1 dessert, pears
- 1 glass sweet milk
- 2 cakes

Breakfast 12/24/36

- 1 bowl oatmeal
milk and sugar
- 4 slices bread
- 1½ slice butter
- 1 apple
- 2 cups coffee
milk and sugar

Lunch

- 4 slices bread
- 1 serving potatoes
- 1 serving cabbage
- 1 serving gravy
- 2 wieners

Supper

- 1 bowl beans
- 3 slices bread
- 1½ slice butter
- 2 slices sausage
- 1 glass sweet milk
- 1 dessert, pudding

Breakfast 12/25/36

- 1 bowl cornflakes
milk and sugar
- 1 egg
- 5 slices bread
- 1½ slices butter
- 2 cups coffee

Christmas Dinner

- 8 slices bread
- 1 serving of cranberries
- 1 serving of turkey
- 1 serving of dressing
- 1 serving of peas
- 2 servings of potatoes
- 3 servings of gravy
- “Eating all Day”
- Ice cream and cake, nuts, candy,
raisins

Breakfast 12/26/36

- 1 bowl farina
milk and sugar
- 4 slices bread
- 1½ slices butter
- 2 cups coffee
- 1 orange

Lunch

- 1 serving peas
- 1 serving potatoes creamed
- 2 wieners
- 4 slices of bread with gravy

Supper

- 2 bowls peas
onions
- 1 slice bologna
- 5 slices bread
- 2 slices butter
- 1½ glass milk
- 1 rice pudding
- 1 orange

Breakfast 12/27/36

- 1 bowl cornflakes
milk and sugar
- 1 egg
- 4 slices bread
- 1 slice butter
- 1 orange
- 2 cups coffee

edema, headache, and albumin in the urine. There were six patients in this series who had evidence of nephritis or hypertension on admission, four were placed on augmented diet and two on regular diet. All six showed a progressive increase in symptoms and were included in the toxic series. Since no strikingly consistent differences were found in the figures for the above enumerated analyzed constituents only a graphic representation of the values averaged for each of the above groups is given in the figures below (Charts 1, 2, and 3). The analytical results for each individual were tabulated by the above designated four groups. Within each group and for each item the

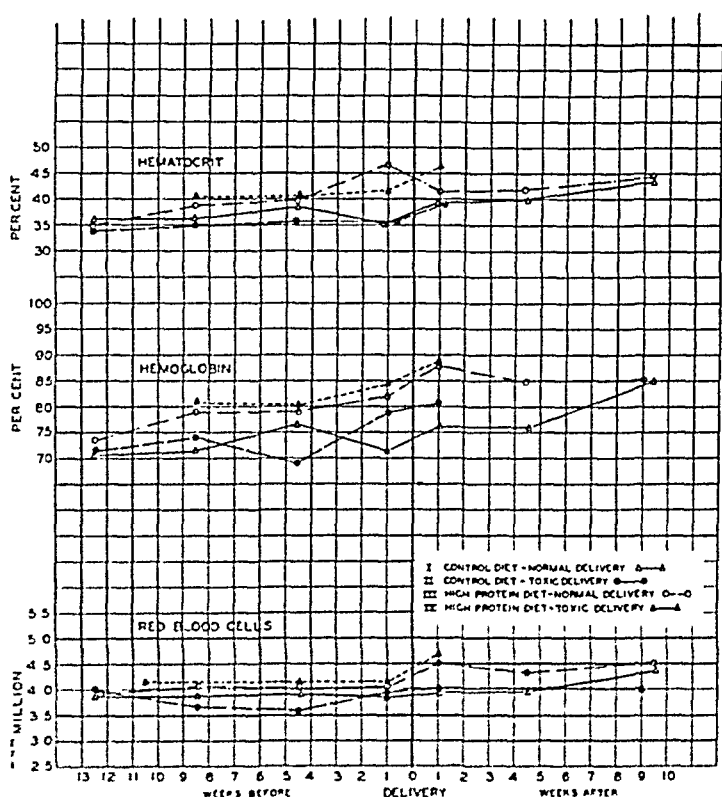


Chart 1.

figures were averaged as they fell into the following periods: antepartum sixteenth through eleventh week, tenth through seventh week, sixth through third week, second through parturition, parturition first two weeks, next four weeks, and next four weeks through the tenth week postpartum. The points given in the figures are averages so obtained.

DISCUSSION OF CHEMICAL DATA

A. *The Hematologic Data.*—(Chart 1.) The red blood cell count, hemoglobin, and hematocrit, while not showing very great differences for the groups, do show: (1) The frequently observed lowering of all of these values, probably due to dilution of the blood as suggested by Dieckmann and others,²⁴ with a return towards normal levels postpartum; and (2) a tendency to the lowest values observed in this study

For these reasons it was decided to add to the diet of every other patient in order of admission the following constituents:

- 150 gm. of skimmed milk powder.
- 20 yeast tablets.
- 15 drops of percomorphum oil.
- 2 gm. of bone meal.
- 4 gm. of ferrous sulfate.

These items supplied to each other patient furnish additional: protein 60 gm., carbohydrate 75 gm., fat 2.5 gm. a total of 580 extra calories, and also adequate amounts of vitamins A, B, D, and E as well as of minerals, particularly of calcium phosphorus and iron. The extra protein supplied by the milk is generally considered to be of high "biological value" particularly for growth of new tissue and the formation of milk in lactation. The dried milk was fed either in the form of a custard or a beverage. In order to avoid jealousy and ill feeling on the part of the inmates not receiving the supplementary items, these items were deliberately not made particularly attractive in the form they were served.

The clinical records of these patients are recorded elsewhere. For purpose of the chemical study samples of blood of the patients were secured on admission, usually fourteen to ten weeks before term, every two weeks thereafter, including one sample a few days before delivery, one shortly after delivery, and at two weekly intervals for ten weeks after delivery. Heparin (Hoffman-LaRoche) was used as an anticoagulant.

On these samples the following determinations were made: hemoglobin (Sahli method), red blood cell count, hematocrit, total protein, albumin by a macromodification of Howe's method²² and nonprotein-nitrogen of the plasma by the usual Folin-Wu method, total fat by Wilson and Hanner's method,²³ the iodine number of the fat by Yasuda's method,²⁴ cholesterol by Schapiro, Lerner and Posen's modification of Schönheimer and Sperry's method,²⁵ phospholipids by a combination of the digestion technic of King,²⁶ and the colorimetric determination of the phosphorus by the method of Fiske and Sabbarow.²⁷

These particular chemical values were selected in the hope that they would reflect the nutritional influences of the diet upon the maternal organism more closely than the others which had been previously studied in normal pregnancy and in toxemias.

For purposes of summarizing the results of these studies, they were treated in four groups on the basis of diet and type of delivery.

- Group I: Control diet, normal delivery, 15 cases.
- Group II: Control diet, toxic delivery, 11 cases.
- Group III: Enhanced diet, normal delivery, 18 cases.
- Group IV: Enhanced diet, toxic delivery, 9 cases.

Toxic delivery means that the patient had signs and symptoms of late toxemia at the time of delivery, elevation in blood pressure to 140/90,

pregnant women. This decrease is almost entirely at the expense of the osmotically more active albumin fraction, and is thus reflected in the figure for colloid osmotic pressure.

An examination of the plasma protein curves for the four groups reveals that the ingestion of the extra milk protein, vitamins, and salts had no appreciable effect on the general level, with the notable exception that immediately antepartum Group II of 11 patients on the control (low protein) diet, who developed toxemic symptoms, also showed on the average the lowest proteins (total protein 5.8 per cent, albumin, 3.05 per cent, globulin [by difference] 2.75 per cent, A/G ratio 1.1, osmotic

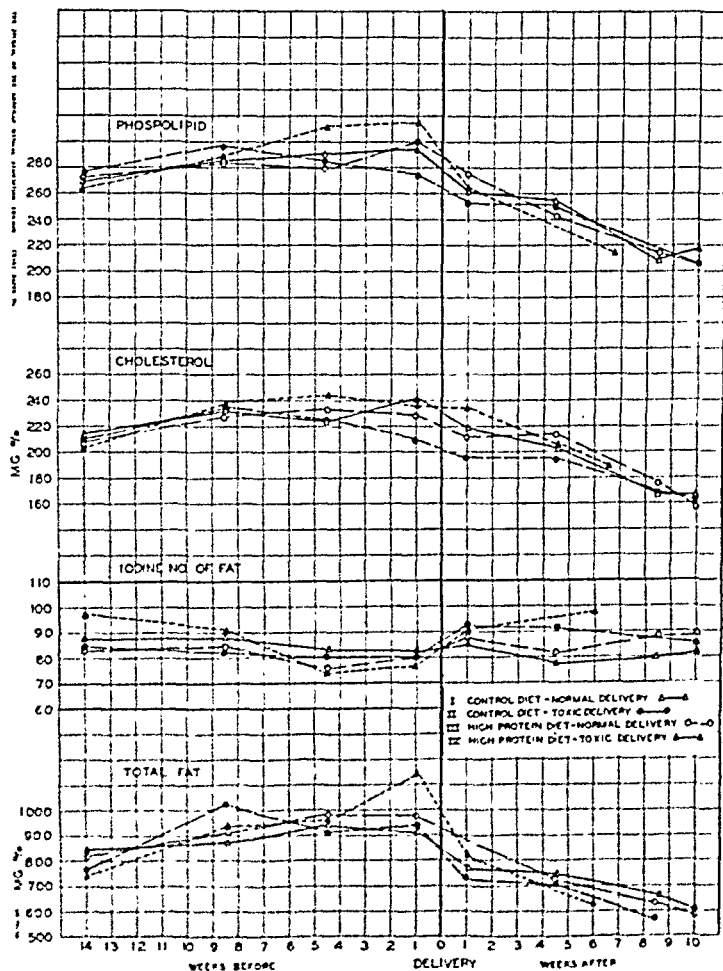


Chart 3.

pressure [calc.] 228 cm. H_2O). It should be noted, however, that Group IV of 9 patients on the high protein diet, who also developed toxemic symptoms, did not show this marked lowering of the plasma proteins as compared with the two groups without toxemic symptoms.

The return of the plasma protein values towards a normal level regardless of type of diet and in spite of the drain of lactation and nursing in this series is quite remarkable and is indicative perhaps of the possibility that the basic control diet used was quite adequate to maintain a normal plasma protein level. It will be noted also that the relative rate of increase of the concentration of the plasma proteins postpartum was much greater than the rate of increase in the hemoglobin and red blood cells. This observation points toward an essential difference in the

in the antepartum period for the two groups on the control (lower protein) diet and consistently higher values for the two groups on the protein and vitamin reinforced diet.

B. *The Plasma Protein and Albumin Data.*—(Chart 2.) Here we observe the general tendency for low protein values, the figures averaged for all four groups at fourteen weeks antepartum are compared in Table VI with the average values at ten weeks postpartum and with the accepted average values for the plasma proteins of normal nonpregnant women as given by Peters and Van Slyke.²⁹ This is more marked in our general series of toxemia patients and was noted by Dieckmann³⁰ who ascribed it to a probable nutritional basis.

The colloid osmotic pressure of the proteins was calculated according to the formula proposed by Wells, Youmans and Miller³⁰ for purposes of comparison with Strauss's data.¹

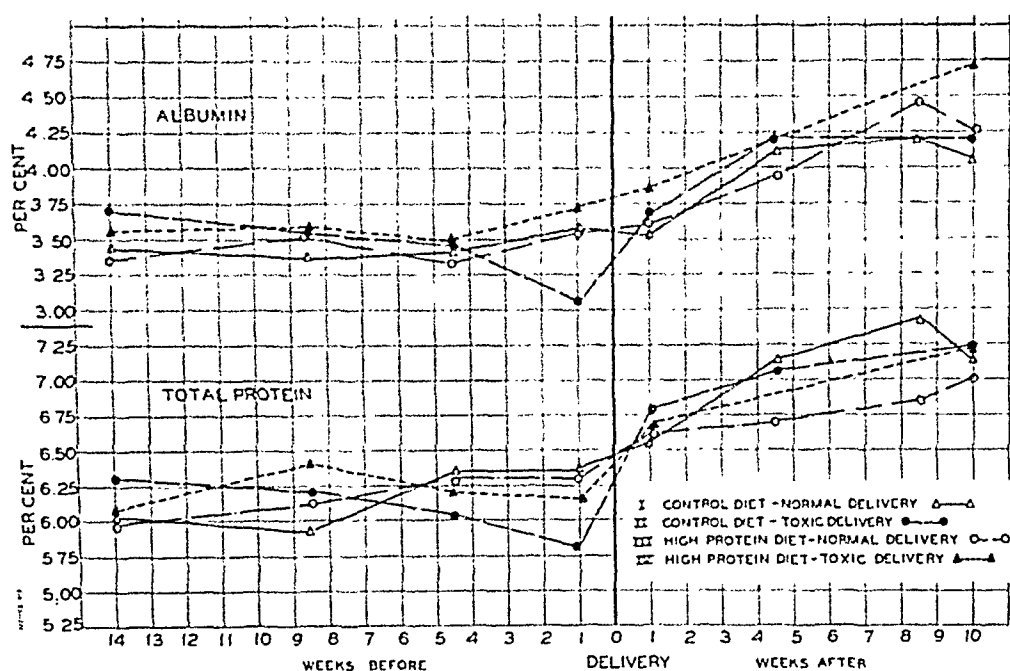


Chart 2.

Our figures for the plasma proteins in the fourteenth week antepartum agree fairly well with those found in the literature (ably reviewed by Dieckmann and Wegner³¹ showing a general decrease as compared with values for normal non-

TABLE VI

	AVERAGE 14 WEEKS ANTEPARTUM 29 CASES	AVERAGE 10 WEEKS POST PARTUM 19 CASES	AVERAGE NONPREGNANT WOMEN (9) 16 CASES
Total protein, gm. per cent	6.1	7.1	7.0
Albumin gm. per cent	3.5	4.3	4.3
Globulin gm. per cent (by difference)	2.6	2.8	2.7
A/G ratio	1.35	1.53	1.59
Colloid osmotic pressure, cm. H ₂ O	256	330	328

ably lies in the fact that the basic diet upon which these additional desirable dietary factors were superimposed was not in the true sense of the term a deficient one.

We wish to thank Dr. Warren Cox, Jr., and the Mead Johnson Company for their generosity in supplying the supplemental diet; Miss Rachel Stephen and Mrs. McClees for their technical aid and the staff of the Salvation Army Maternity Home for their cooperation.

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mechanisms of the apparent regeneration of the plasma proteins and of the red blood cells apart from the mechanical factor of the increased hydremia antepartum, designated as "oligocythemie hypervolemia" by Dieckmann and Wegner.²⁸

C. *The Plasma Fate and Lipin*.—The curves in Chart 3 for the average values in the four groups confirm in general the established tendency towards hyperlipemia in pregnancy. This subject was recently reinvestigated and reviewed by Boyd.³² While, in common with other observers, large individual variations were found in this study in all four groups, the total lipin, cholesterol and phospholipid values, already considerably above normal levels at the beginning of our observations in the fourteenth week antepartum, tended to increase still further until parturition and fall to normal levels postpartum. No striking differences were found which could be accounted for either on the basis of diet or of presence or absence of toxemic symptoms. The only general observation which can be made is that in pregnancy, as in other conditions involving hypoproteinemia notably in nephrosis and in other forms of water retention, there appears to be a tendency towards a concomitant hyperlipemia. This may or may not be an expression of an attempt on the part of the organism to compensate for the fall in the colloid osmotic pressure due to the hypoproteinemia as suggested by Fishberg.³³ But as pointed out by Boyd³² the true cause of hyperlipemia of pregnancy is still obscure. The curves of the iodine number values of the total plasma fat appear to vary inversely as the values for the total fats. This indicates that the increase antepartum and the fall postpartum in the plasma fatty acids is largely accounted for by the saturated fatty acids, as was previously observed in a study of the lipins in hyperthyroidism by Nicholls and Perlzweig.³⁴ This undoubtedly points to changes in the ratio of saturated to unsaturated plasma lipins, but the significance of this factor for the physicochemical equilibrium of the blood is as yet not clear.

The weight gain over a period of three months antepartum averaged 15 pounds in the group receiving the augmented diet and 12 in the regular diet group. Edema was noted more often in the latter group.

There was little difference in the blood pressure readings of the two groups. As a rule, it was low, 100 to 114 systolic and 60 to 70 diastolic. In the toxemia group we naturally found an increase of pressure, more pronounced in the diastolic figure, as well as an unusual weight gain—in one instance 50 pounds in three months.

CONCLUSIONS

Puerperal albuminuria and eclampsia account for the highest percentage of maternal deaths in North Carolina.

Lack of prenatal care is the prime factor in these deaths.

The incidence of toxemia of pregnancy and nutritional diseases parallel in this state.

It appears from this study on 54 young primiparae that the addition of dried milk, vitamins, calcium, and iron to a diet which may be regarded as marginal in regard to protein, vitamins and minerals did not exert an appreciable effect on the incidence of toxemic symptoms. Nor were there observed any significant effects upon the blood cells, hemoglobin, and dilution, nor upon the concentration of the plasma proteins, fats, and lipids. The most likely explanation for this prob-

after delivery, thus permitting several observations on each individual. Routine determinations included height and weight, respiratory rate, total volume of respired air per unit of time, and the CO_2 and O_2 content of the expired air. These data permitted calculation of the minute volume of respired air, and the amount of the tidal air, while the CO_2 produced and the O_2 absorbed were computed per kilogram of body weight and per square meter of body surface area. The ratio between the minute volume of respired air and the total CO_2 produced per minute was used as an index of the degree of hyperventilation.

Table I shows that there was little change in the respiratory rate during the thirty weeks of pregnancy for which average values are available, but that during the same interval the tidal air increased by approximately 28 per cent (from 265 to 339 c.c. per respiration). The minute volume of air passed through the lungs increased 26 per cent, although in terms of square meters of body surface the increase was only 11 per cent, and in terms of kilograms of body weight it was insignificant. The ventilation ratio remained practically constant, although as compared with values obtained in the late puerperium there was a considerable increase. Apparently the respiratory changes incident to pregnancy make their appearance in the very early weeks after conception.

Associated with these alterations in ventilation, there were definite changes in the composition of the expired air. The percentage of CO_2 remained at a low level (3.03 to 3.15 per cent) from the 12th to the 40th week of pregnancy, whereas in the postpartum period it approached the normal nonpregnant level, ranging from 3.30 to 3.98 per cent. There was an associated rise in the amount of CO_2 expired per minute and per square meter of body surface, although the amount per kilogram of body weight was scarcely altered.

The percentage of O_2 absorbed decreased slightly from the twelfth week of pregnancy, when it was already considerably below the nonpregnant level as represented by readings obtained after the second postpartum week. At the same time, the absolute amount of O_2 absorbed per minute increased during pregnancy and fell again after delivery. When calculated per kilogram of body weight, the absorption of O_2 was highest in the third and fourth lunar months of pregnancy, gradually decreased during the remainder of gestation, and showed a further fall in the postpartum period. On the other hand, the absorption of O_2 per square meter of body surface increased slightly from the twelfth to the fortieth weeks of pregnancy and then fell rather considerably after delivery.

It is postulated that these unexpected variations in gaseous exchange may be due to the fact that the rapid increase in body weight during gestation is due largely to fat deposition and water retention. The

RESPIRATION AND PULMONARY VENTILATION IN NORMAL NONPREGNANT, PREGNANT, AND PUERPERAL WOMEN*

WITH AN INTERPRETATION OF THE ACID-BASE BALANCE DURING
NORMAL PREGNANCY

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THE total respiratory metabolism in pregnant and nonpregnant women has been thoroughly studied, but little attention has been directed toward associating the altered respiratory gaseous exchange with the acid-base balance during gestation.

Magnus-Levy,¹ Zuntz,² Klaften,³ Rowe, Gullivan, and Matthews,⁴ Schroeder,⁵ and Berconsky and Rossignoli⁶ have shown that the amount of air respired per minute increases progressively during pregnancy but returns to normal levels promptly after delivery. These reports also indicate that there is usually a slight increase in the respiratory rate, associated with a more marked increase in the tidal air (the volume of air involved in a single respiration). Certain of these investigators^{1-3, 6} found that the percentage of CO₂ in the expired air remains quite constant during gestation, while the minute volume of CO₂ produced increases. It has also been observed that the percentage of O₂ absorbed from the inspired air is diminished slightly, although the total volume absorbed per minute is increased, thereby producing variable and probably insignificant variations in the volume of O₂ absorbed per minute per kilogram of body weight.

The present communication offers further data on the respiratory gaseous exchange in pregnant and early puerperal, as compared with normal, nonpregnant women, and attempts to interpret the acid-base balance of the blood during pregnancy in terms of alterations in the respiratory exchange.

The interest of one of us (E. D. P.) in this problem developed from a critical survey of data compiled during an earlier investigation of the basal metabolism during pregnancy,⁷ using the method described by Bailey,⁸ which is essentially that of Boothby and Saniford.⁹ The expired air was collected in a Tissot spirometer, and the CO₂ and O₂ were determined in duplicate with the Henderson-Haldane gas-analysis apparatus. All tests were made in the morning after ten to twelve hours fasting and after a preliminary rest period. A total of 290 determinations were made on 56 normal pregnant and puerperal women. These patients usually reported at four-week intervals during pregnancy, in many instances from the third lunar month, and at seven-day intervals

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slight increase in oxygen absorption and in carbon dioxide production per square meter of surface area explains the moderate rise in the basal metabolic rate during the latter half of pregnancy and may be related to the metabolism of the rapidly growing fetus.

Since these older values were calculated from work sheets prepared in the routine performance of basal metabolism tests by trained technicians, it was thought wise to repeat the work under research conditions. The original technic was followed as closely as possible and all determinations were made by one of the authors (F. W. O.). Obstetric patients were available only during the last month of pregnancy and for the first ten days after delivery. Twenty-two normal primigravidae and 23 multigravidae were studied before delivery and 10 primiparae and 11 multiparae after delivery. In addition, 20 normal nonpregnant women (nurses and laboratory technicians) were available as controls.

The average results are recorded in Table II. The minute volume of respired air is markedly increased over the nonpregnant average (45 per cent in the primigravidae and 43 per cent in the multigravidae). This increased air exchange is associated with a rise in the tidal air, even though the respiratory rate is increased from 14 to 16.5 (average) per minute. The percentages of O_2 absorbed and of CO_2 produced are decreased, probably as a result of the augmented air exchange, while the volumes exchanged per minute are increased. There is also an increase in the volume of gaseous exchange per square meter of body surface and per kilogram of body weight. The ratio of the minute volume of respired air to the volume of CO_2 produced (an index of the degree of hyperventilation) rises from 31.2 in the nonpregnant to 35.4 in each group of pregnant women, an increase of 4.2 c.e., or 13.4 per cent.

The data show relatively little difference between primigravidae and multigravidae, except that both the total gaseous exchange and the tidal air are slightly greater in the former.

In the puerperal women (five to ten days after delivery) the average values tend to approach the nonpregnant level, which in certain instances is actually reached.

While there are certain differences between the two series, they are in general confirmatory, and demonstrate that there are certain consistent changes in gaseous exchange during gestation: (1) The tidal air increases, contrary to the popular belief that the upward pressure of the pregnant uterus restricts the capacity of the chest cage. Apparently the lateral expansion of the chest wall more than compensates for the upward displacement of the diaphragm. (2) More air passes through the lungs per unit of time. This is an expression of the increased tidal air plus the increase in the respiratory rate. (3) The O_2 absorption and the CO_2 production per unit of time, per minute per kilogram of body weight, and per minute per square meter of body surface are increased during pregnancy, but the increased pulmonary

TABLE I. THE RESPIRATORY GASEOUS EXCHANGE IN NORMAL NONPREGNANT, PREGNANT, AND PUERPERAL WOMEN.
(HENRY FORD HOSPITAL SERIES) (AVERAGE VALUES)

MATERIAL	NUMBER OF DETERMINATIONS	kg.	VENTILATION										CARBON DIOXIDE EXPIRED						OXYGEN ABSORBED	
			BODY SURFACE AREA	RATE OF RESPIRATION	PER MINUTE	liters	ml.	PER MINUTE PER KILOGRAM OF BODY WEIGHT	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA	TIDAL AIR	VENT. CO ₂ PER MIN.	per cent	ml.	PER MINUTE PER KILOGRAM OF BODY WEIGHT	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA	FROM RESPIRED AIR	per cent	ml.	PER MINUTE PER KILOGRAM OF BODY WEIGHT	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA
Pregnant (Weeks after last menstrual period):	14	53.5	1.53	18.4	4.88	91.1	3.19	265	32.5	3.08	150	2.81	98	4.74	232	4.33	151			
iii (Ninth to twelfth incl.)																				
iv (Thirteenth to sixteenth incl.)	28	55.2	1.57	18.3	5.04	91.2	3.22	275	32.3	3.10	156	2.83	100	4.72	238	4.31	152			
v (Seventeenth to twentieth incl.)	43	58.9	1.60	18.4	5.23	88.9	3.25	284	32.6	3.06	160	2.72	100	4.60	241	4.08	150			
vi (Twenty-first to twenty-fourth incl.)	44	60.1	1.62	18.5	5.33	88.6	3.29	288	31.9	3.13	167	2.78	103	4.66	249	4.13	153			
vii (Twenty-fifth to twenty-eighth incl.)	46	62.4	1.65	18.4	5.50	88.2	3.34	299	32.3	3.10	170	2.73	103	4.54	249	4.00	152			
viii (Twenty-ninth to thirty-second incl.)	40	65.0	1.67	18.6	5.80	89.3	3.47	312	32.2	3.10	180	2.77	108	4.50	261	4.02	155			
ix (Thirty-third to thirty-sixth incl.)	43	66.8	1.70	18.7	6.05	90.5	3.56	323	31.9	3.15	190	2.85	118	4.51	273	4.08	160			
x (Thirty-seventh to fortieth incl.)	32	66.6	1.69	18.5	6.17	92.6	3.65	339	33.0	3.03	187	2.80	111	4.36	269	4.04	159			
Puerperal (Weeks after the delivery):																				
First	29	60.2	1.62	17.5	5.18	86.1	3.20	296	30.3	3.30	171	2.84	105	4.66	242	4.02	150			
Second	52	59.6	1.60	17.3	4.66	78.2	2.90	270	28.6	3.50	163	2.74	102	4.85	226	3.80	141			
Third	26	58.2	1.60	16.8	4.20	72.2	2.62	250	25.1	3.98	167	2.87	104	5.15	216	3.72	135			
Fourth, fifth, sixth	6	56.0	1.58	18.3	4.20	75.0	2.66	230	27.6	3.62	152	2.75	96	5.00	210	3.75	133			
Seventh to fourteenth incl.	12	60.2	1.61	17.7	4.40	73.2	2.73	248	28.6	3.49	154	2.55	95	5.11	225	3.74	140			

ventilation leads to a significant reduction in the percentage of oxygen absorbed from and of carbon dioxide added to the air during its passage through the lungs. (4) The ratio of air respired per minute to the CO_2 expired per minute indicates a considerably increased pulmonary ventilation, which appears in the first trimester of pregnancy and disappears during the first two weeks after delivery.

DISCUSSION

Divergent interpretations of the acid-base balance during pregnancy have been presented by two groups of investigators,^{10, 11} although it is generally agreed that gestation is accompanied by a fall in the serum bicarbonate content and in the alkaline reserve. Zuntz,² Magnus-Levy,¹ and Schroeder⁵ noted a definite increase in the minute volume of respired air, while Hasselbalch and Gammeltoft,¹² Rowe,¹³ and others,^{14, 15} have shown that the CO_2 tension of the alveolar air is reduced. Bokelmann and Rother¹⁶ have reported that the urine is slightly more alkaline in pregnant than in puerperal women. Stander, Eastman, Harrison, and Cadden¹⁷ found no increase in organic acids or any evidence of the presence of unusual acids in the blood during normal pregnancy. Reported values for the pH of plasma are not in agreement, certain observers recording the hydrogen ion concentration slightly lower than the normal average and others detecting no significant variation.

Muntwyler, Limbach, Bill, and Meyers¹⁸ found the blood pH of normal antepartum women usually slightly above the nonpregnant level and concluded that hyperventilation is responsible for the change. They believe that hyperventilation causes the CO_2 to be lowered while the base diminishes secondarily as a compensatory reaction.

On the other hand, Kydd, Oard, and Peters¹⁹ object to the assumption that the fall in bicarbonate results from hyperventilation, and offer the following specific criticisms: (1) They, and certain other observers, find that the blood pH values of pregnant women are not elevated. (2) Muntwyler and others studied such heterogeneous material that their average figures are of little significance. (3) The observation of Muntwyler and others, that the elevated pH persists for some days after delivery, although the total base and the CO_2 content have returned to normal levels, would seem to invalidate their theory concerning the CO_2 and base deficits, since the high pH would indicate that the hyperventilation persists after disappearance of the CO_2 deficit, which it supposedly has induced. (4) It has not yet been demonstrated that the CO_2 deficit of hyperventilation is compensated for by reduction of base. Experiments by Peters, Bulger, Eisenmann, and Lee,¹⁹ and others,^{20, 21} indicate that compensation for such a CO_2 deficit is established by an increase in the chlorides without a change in the total base.

The data here presented tend to confirm the contention that the pulmonary hyperventilation, which is physiologic in pregnant woman, must be a factor in the regulation of the acid-base balance. Due to the gradual development of the increased respiratory exchange and its long duration, a new acid-base equilibrium is established, in which the tendency toward an elevated pH is compensated for by a decrease in the

TABLE II. THE RESPIRATORY GASEOUS EXCHANGE IN NORMAL NONPREGNANT, PREGNANT, AND PUERPERAL WOMEN.
(UNIVERSITY OF IOWA SERIES) (AVERAGE VALUES)

MATERIAL	NO. OF DETERM- NATIONS	kg.	sq.m.	RATE OF RESPIRATION PER MINUTE	VENTILATION								CARBON DIOXIDE EXPIRED						OXYGEN ABSORBED		
					liters	ml.	PER MINUTE PER KILOGRAM OF BODY WEIGHT	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA	TIDAL AIR	VENT. CO ₂ PER MIN.	IN EXPIRED AIR	ml.	PER MINUTE PER KILOGRAM OF BODY WEIGHT	ml.	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA	FROM RESPIRED AIR	PER MINUTE	PER MINUTE PER KILOGRAM OF BODY WEIGHT	PER MINUTE PER SQUARE METER OF BODY SURFACE AREA		
Nonpregnant	20	55.8	1.58	14.0	4.68	84.0	2.96	334	31.2	3.31	150	2.78	95	4.39	206	3.69	130				
Late pregnant	22	63.1	1.64	16.3	6.78	107.3	4.13	416	35.4	2.83	192	3.04	117	4.04	274	4.34	167				
Primigravidae	23	64.2	1.66	16.9	6.70	104.3	4.04	396	35.4	2.83	189	2.96	114	4.04	271	4.21	163				
Multigravidae																					
Puerperal	11	52.9	1.51	16.5	5.17	97.8	3.42	313	33.6	2.99	154	2.92	102	4.07	210	3.97	139				
Primiparae	10	63.4	1.67	16.7	5.57	87.9	3.33	333	32.0	3.12	174	2.74	104	4.18	233	3.68	139				
Multiparae																					

alkali in the blood is gradually excreted through the kidneys, producing a less acid urine and resulting finally in the restoration of the normal acid-base balance.

In normal pregnant women, the hyperventilation is mild and continues over several months, during which the bicarbonate is decreased in proportion to the reduction of the CO_2 content, and the blood maintains a normal pH. When, as in some of the cases reported by Muntwyler and others,¹⁸ the blood pH is above normal, it would seem reasonable to assume some interference with the usual compensatory reduction of the concentration of bicarbonate, although it is to be expected that this protective mechanism would be operative and effective in the majority of normal women.

Our data indicate that the physiologic hyperventilation of pregnancy does not cease abruptly with delivery, but disappears gradually during the first two weeks of the puerperium. This observation probably explains the findings of Muntwyler and others¹⁸ who noted a slightly elevated pH in certain women after delivery, even though the bicarbonate and total base had returned to normal, and there was a slight increase in the total acids of the blood.

SUMMARY

1. The respiratory rate is increased slightly from the fourth lunar month of gestation to term.
2. The volume of tidal air and the minute volume of respired air increase progressively during pregnancy and return to normal during the second week after delivery.
3. The minute volumes of CO_2 produced and of O_2 absorbed increase gradually during pregnancy and approach the normal nonpregnant level from one to two weeks postpartum.
4. The ratio of the minute volume of respired air to the CO_2 expired is greater in pregnant than in nonpregnant women. One week after delivery this ratio is less than during pregnancy but still greater than in nonpregnant controls.

CONCLUSION

The acid-base balance of the blood of normal pregnant women represents a condition of compensated CO_2 deficit due to physiologic hyperventilation. The long period of pregnancy results in an equilibrium in which a potentially increased pH, due to hyperventilation, is returned to normal by a lowered plasma bicarbonate and a proportionately decreased carbonic acid.

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plasma bicarbonate proportional to the lowering of the carbon dioxide. This compensatory development serves generally to maintain the hydrogen ion concentration within recognized normal limits.²²

The increased volume of respired air in terms both of body weight and of surface area indicates hyperventilation, as do the accelerated respiratory rate and the increased volume of tidal air. Available data suggest strongly that the hyperventilation is due not to an increased production of CO_2 by a physiologic acceleration of metabolism, but rather to some other stimulus which increases the respiratory exchange and secondarily lowers the CO_2 tension. It should be noted that the ratio of the volume of respired air to that of the CO_2 produced is greater in pregnant than in nonpregnant women, i.e., more air is respired during the removal of a given amount of carbon dioxide. Moreover, Stander and others¹⁷ have shown that there is no increase in organic acids and no accumulation of abnormal acids in the blood of pregnant women which might cause a compensatory hyperventilation. Hydrogen ion determinations also indicate that there are no unusual acids in the circulating blood. Consequently the only known acid which might be responsible for the respiratory alteration is carbonic acid, which, however, is at a lower than normal level in the blood of pregnant women.

The term "hyperventilation," as used in connection with "acid-base balance," is somewhat confusing since it may refer either to forced respiration over a comparatively short interval, producing a picture of alkalosis, or to an accelerated respiratory rate caused by an increased concentration of hydrogen ions. In either instance, the respiratory rate and the minute volume of respired air are increased and the alveolar CO_2 is reduced. It is well recognized that when the hydrogen ion concentration of the blood is increased, as in uncompensated acidosis, the respiratory center is stimulated and the respiratory exchange is accelerated to "blow off" carbon dioxide. This mechanism alters the ratio between the bicarbonate and the free CO_2 of the blood and thus tends to restore the normal hydrogen ion concentration. When the low pH is due to acids other than carbonic, the resultant hyperventilation "blows off" the carbon dioxide producing very low CO_2 tensions in the blood and alveolar air without materially affecting the hydrogen ion concentration of the blood.

The fact that there is no increase in acids in the blood in normal pregnancy leads to the conclusion that the hyperventilation during gestation is not due to an increased hydrogen ion concentration, i.e., an acidosis, but rather to some unknown stimulus. Hyperventilation produced by stimuli other than an increased acidity can lower the CO_2 tension, as is demonstrated in experiments involving voluntarily forced respirations, when the ratio of bicarbonate to free carbonic acid is disturbed and the blood pH rises promptly, due to the fact that the bicarbonate decreases less rapidly than the carbon dioxide. The excess

tion for investigations of the utmost practical value. If I may say so, it is my firm conviction that this association and American obstetricians in general need more studies on fundamental problems such as these two you have just heard.

DR. PAUL TITUS, PITTSBURGH, PA.—In every research problem carried out so thoroughly as this one has been, I like to look for the practical clinical application of the findings. Plass and Oberst have presented certain specific facts to you; namely, that the pregnant woman's respiratory rate increases progressively from the fourth month onward, as does also the volume of each respiration. They have reasoned logically that this is as physiologic as it is for any of us to breathe more rapidly and more deeply whenever we exert ourselves physically more than usual. When the pregnant woman's race is over, these, with their concomitant blood chemistry changes, quickly return to their normal nonpregnant level.

A clinical conjecture is suggested by this work. Does it not indicate that basal metabolism estimations made in the first four months of pregnancy would show fairly truly the state of a pregnant woman's thyroid and pituitary activity? Those taken later, however, would need to be discounted by perhaps 10 or 15 per cent due to this physiologic reaction shown by the authors. In other words, the pregnant woman is never in a resting state, and even a normal basal metabolic rate might be the expected finding in a patient actually suffering from thyroid deficiency, and requiring medication. Similarly, a woman showing high basal metabolism readings toward the close of her pregnancy should not be thought to have an overactive thyroid unless other clinical signs of this are present.

DR. FOSTER S. KELLOGG, BOSTON, MASS.—Dr. Ross' figures supply me with an answer to a troublesome question. Why does the South know more about eclampsia than we do? How does Dr. Rucker, not to mention others, see so much eclampsia when it takes our hospital twenty years to get a series of 173 cases? The answer is simple—there is more there to see.

Further, we have sometimes said to ourselves that if the mortality results reported from the Southern institutions are so much better than ours the condition called eclampsia must be milder there. But the terrific general mortality from toxemia as reported by Hamilton, and quoted by Ross, 43 per cent of the puerperal deaths in North Carolina in 1933, shows that this is probably not true. Hence, I must conclude that in the South those toxemic patients with convulsions are being cured by treatment who get to the hospital soon enough. To date we have only lowered our number of deaths from this cause by preconvulsive interference. I have the hope that by adopting your experience we shall do better.

One interesting reason for the discrepancy of the results is brought out in Ross' paper and seems worth comment. He writes that, "We have found urinary infection and essential hypertension in the private patient group more often than in the lower stratum where we have found eclampsia." Our own figures show a maternal mortality of 40 per cent in a known nephropathic (including essential hypertension) group of eclamptics, as against a 10 per cent mortality in a known nonnephropathic group. By implication at least the bulk of these lower stratum eclamptics are what I have called "toxemias of neglect" and elsewhere I have pointed out that toxemias of neglect, treated within a reasonable time, show better results than toxemias developing in spite of good care, which are prone to occur on a hypertension or kidney background.

This paper seems to show that the essence of prevention of eclampsia lies in the timeworn prescription of prenatal care. That it is efficient no one controverts; that its practical application in certain rural communities has not yet been established seems evident. Possibly taxes diverted from the digging of holes and refilling of same to a broad prenatal care program would be profitable.

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DISCUSSION ON PAPERS BY DRS. ROSS AND PLASS

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD.—Of the several changes which take place in the blood during pregnancy, the reduction in the carbon dioxide content of the serum is one of the most constant. Since the report by Oard and Peters in 1929, it has been known that this fall in carbon dioxide is paralleled by a diminution in the total base of the serum. This reduction amounts to about 8 mm., or 5 per cent.

Dr. Plass has now shown us very clearly that a marked degree of hyperventilation occurs in pregnancy and postulates that this causes both the fall in the carbon dioxide content of the serum and the fall in total base. That hyperventilation causes the fall in carbon dioxide is plausible enough since part of the carbon dioxide is present as free carbonic acid gas and could be easily blown off. But whether it is also responsible for the fall in the basic radicles is a more difficult question. The chronic hyperventilation which occurs in persons living at high altitudes is not dissimilar to that seen in pregnancy, and it would seem of interest to inquire into total serum base behavior under these circumstances. The person living at a high altitude breathes faster and deeper in order to get enough oxygen from a rarefied air; the pregnant woman breathes faster and deeper in order to get enough oxygen for her increased blood volume and increased minute output of her heart. Recently Dill and his associates have shown that the most notable change in the electrolytes of the blood at high altitudes is a decrease in the carbon dioxide content. He reports a reduction of 8 mm. This decrease in carbon dioxide is partially balanced by an increase of 4 mm. in serum chloride and a decrease of 2 mm. in sodium, leaving an unexplained anion deficit of about 2 mm. The pH increased slightly. If hyperventilation can cause even this slight decrease in total base at high altitudes, it seems altogether likely that it is responsible for a substantial part or possibly all of the reduction in total base seen in pregnancy. There may be other factors such as blood dilution.

I agree with Dr. Plass that there is no increase in organic acids and no appreciable change in blood pH during normal pregnancy.

In conclusion, I should like to make a few remarks about studies of this general type. When a paper such as this is presented before a clinical group the question naturally arises, what is the practical value of this paper? You will remember when Benjamin Franklin demonstrated electricity to the French salons in Paris their first question was, what is the practical value of this thing you call electricity? And you will remember his famous reply: "Of what practical value is a newborn baby?" And so it is with a work of this type. Although at present it may not seem to have much practical value, there is reason to believe that when work of this type is pieced together the various studies will form a mosaic which will serve as a founda-

such a concept is logical if one takes the view that the symptoms of toxemia are largely the result of efforts on the part of the organism to protect itself. The eclamptic convulsion represents an ideal mechanism for developing an acidosis. When the convulsion begins, respiration stops, and carbon dioxide accumulates in the body. Moreover, the violent muscular contractions with a lack of oxygen lead to the production of relatively large quantities of lactic acid, through the incomplete oxidation of dextrose. The eclamptic convulsion is thus an ideal mechanism for overcoming an alkalosis. A further fact which supports the same idea is that all of the drugs, with the exception of *veratrum viride*, which have been used successfully in the treatment of eclampsia are respiratory poisons. This includes morphine chloral, magnesium sulphate, and the various barbiturates. Treatment of eclampsia with any of these drugs is not effective unless the respirations are definitely lowered.

DR. ROSS (closing).—We know that our problem is different from that in the East, Midwest and West. Only by careful observation and scrupulous recording can we be of mutual benefit.

Our toxemic group eats an unusual amount of cured or salt pork. It seems paradoxical but the folks living on the farm do not raise their own farm and dairy produce, especially in "good times." The land is used for cash crops and the food brought from stores. During the depression the incidence of eclampsia as well as pellagra was somewhat lower because the farmers had to be self-sustaining.

THE FRANK-GEIST OPERATION FOR CONGENITAL ABSENCE OF VAGINA*

WALTER T. DANNREUTHER, M.D., F.A.C.S., New York, N. Y.

VARIOUS operative procedures have been devised for the construction of a vaginal canal in females whose external genitals are otherwise normal. Surgical interference is justified in a young, attractive girl with obvious secondary sex characteristics and sex urge; in a patient who is contemplating marriage and who understands the existing anomaly; in a married woman who finds it impossible to fulfill her marital obligations; and for the relief of hematometra when there is vaginal aplasia.

Two distinct types of defect come under observation: first, a gynatresia which results from birth trauma; and second, congenital aplasia of the vagina which, as a rule, is associated with absence or rudimentary development of the uterus. In most of the latter group there are normal external genitals, tubes, and ovaries, but complete absence of the uterus and vagina. In these individuals it is evident that during the embryonal period, there was no union of the Müllerian ducts and no formation of the uterovaginal canal.

The first attempts to establish a vaginal canal in such cases consisted of making an opening in the cellular tissue between the bladder

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Our only piece of direct comparison to the results shown in Dr. Ross' paper is this. We selected 80 patients in the clinic upon whom we might try the effect on the blood picture of far better than average diet, including feedings of iron and extra vitamins. Of these 80 patients 17 happened to have come to a preeclamptic or eclamptic end in a previous pregnancy and 7 of them have had eclampsia. Taking the ordinary average of recurrent preeclampsia and eclampsia, we should with only ordinary care have had a certain number develop toxemia, but the result in these 17 patients was that none of them developed any toxemia whatever. It may yet be shown that deficiency diet plays a part in the production of "toxemias of neglect."

DR. M. PIERCE RUCKER, RICHMOND, VA.—Dr. Ross does well to direct our attention to the rôle of diet in the so-called toxemias of pregnancy. It is a complicated subject that needs clarification.

We are told that in Germany during the war, when there was a marked deficiency in food, eclampsia practically disappeared. We are also told that in China, where the mass of people are always on a diet deficient in vitamins and protein, eclampsia occurs not infrequently. Last spring Professor DeSnoo told us that eclampsia was due to excess of sodium chloride. It would be interesting if Dr. Ross can tell us about the salt ingestion of his undernourished North Carolinians.

We have been taught for so many years that we should restrict the diet of a patient with albuminuria and a rising blood pressure, that we starve them almost automatically. It is a question whether it is either wise or even logical. I was particularly interested in the observations that he made in the Salvation Army Home. For years I have been connected with a home for unmarried mothers. Five years ago this home moved from a location near the center of town to a seventy acre farm. There was no change in the personnel of the management. The clientele remained the same. The diet and habits of the girls, however, underwent a marked change. The girls ran the farm, took care of the cows, chickens, pigs, and garden. They had an overabundance of dairy products, eggs, and green vegetables. The dietary before and after the move always contained meat once a day. Since the move there has been only one case of eclampsia, where in the last five years in town there were seven cases. Even more striking has been the change in the incidence of hypertension. In town there was nearly always a "waiting" girl under treatment for this condition. On the farm there is rarely a case.

The close correlation that Dr. Ross finds between the incidence of pellagra and that of the toxemias of pregnancy is interesting. No doubt he would find the same correlation between the presence of pellagra and the absence of prenatal care. We know practically nothing about the cause of eclampsia and preeclampsia. We do know the prodromal symptoms and the preventive treatment, and our empirical treatment has improved wonderfully in the past ten or fifteen years.

DR. E. L. KING, NEW ORLEANS, LA.—Some years ago I found from Italy, Mississippi, and Florida three different papers reporting cases of toxemia with hookworm disease. I then noted the same thing in our Charity Hospital in New Orleans. We found also, that patients with marked anemia as well as hookworm disease, gave us more trouble than those who had hookworm disease alone. In studying the stools we found that 10 per cent of all patients had hookworm disease, while those patients coming from the country must have been from 20 per cent to 25 per cent infested. So that in addition to nutritional deficiencies, the tendency to pellagra, and the low economic status of our patients, there was the complication of the hookworm infestation.

DR. PLASS (closing).—My own interest in hyperventilation arises from my conviction that there is, as a basis for the toxemias of pregnancy, an underlying alkalosis. Obviously this work does not support such a contention. Nevertheless,

coccyx, and separating the rectum from the anterior surface of the sacrum. After stripping the gut from its surroundings, it was drawn into the incision, ligated in two places and cut. The superior portion was separated from the bladder, drawn down to the base and sutured. This superior segment of the rectum was found surrounded by some fibers of the levator ani, which were secured with it to act as a third anal sphincter. The inferior segment was brought down and its upper end closed by sutures, thus forming a culdesac or cavity to serve as the new vagina. A secondary operation was done to establish the vaginal opening fourteen days later. This consisted of making an incision through the fibrous ring situated between the anus and the lower border of the urethra, uniting the rectal mucous membrane to the adjacent parts and transforming the circular opening into a longitudinal one. The description of this operation in the original article is somewhat hazy and just what was done with the anus in this case is not clear from either the text or the illustrations which accompany it. This very early case of Sneguireff's probably served as the basis for the technique proposed by Popow⁶ and which he described in 1910 and had carried out in 5 cases prior to 1914. This was further elaborated upon by Schubert⁷ in 1911.

For many years the most popular and successful operation for the formation of an artificial vagina was that proposed by Baldwin⁸ in 1904, and it is interesting to note that the case which gave Baldwin his concept of the technique which he later perfected occurred in a patient who did not have a congenitally absent vagina, but who had had a sloughing of the entire vagina and cervix following delivery at term by instruments and after craniotomy. Unfortunately this woman refused operation.

Baldwin⁹ did not perform his first operation until March, 1907, when he did it on a woman of thirty-eight years whose vagina had also sloughed out as the result of birth trauma. The Baldwin operation in the hands of most abdominal surgeons, including its originator, has carried with it a 6 to 17 per cent operative mortality. Its most enthusiastic advocates at the present time are Judin,¹⁰ who reported 6 successful cases in 1927, and Masson,¹¹ who reported 5 successful cases in 1932, all 11 cases having been done without a fatality. Briefly the operation consists of the following steps:

1. Dissection of a canal in the soft tissue between the bladder and rectum up to the peritoneum, which is tightly packed with gauze.
2. Resection of a loop in the lower part of the ileum about 25 cm. long with mesentery sufficient to allow it to reach to the perineum.
3. Side-to-side anastomosis to re-establish the continuity of the intestinal lumen.
4. Closure by purse-string suture of the ends of the detached section.
5. Drawing down of the lower point of the loop into the excavation made between the bladder and rectum. (To insure adequate blood supply it is advisable to leave large vessels at each end of the resected loop rather than a single one in the middle where the tension is greatest.)
6. Closure of the abdominal wound.
7. Opening of the presenting loop of bowel in the perineal wound and stitching to the skin of the vulva by interrupted silk sutures.
8. Repacking of the bowel with sterile gauze.
9. Destruction of the septum between the two sections of bowel two weeks later by application of forceps.

and rectum and inserting some form of tampon to maintain its patency. Dupuytren apparently operated upon the first patient in 1817. These early operations were obviously doomed to failure, although Kanter¹ reported a somewhat similar operation in 1935 in an individual who had a partial atresia of the vaginal canal. The treatment consisted solely of repeated dilatations and packing, and two years afterward the vagina was patent and well epithelized from the introitus to the cervix, although abnormally narrow. Kanter's patient had a preoperative vaginal opening which almost admitted the tip of the examining finger for a distance of one inch, as well as a double uterus with normal Fallopian tubes and ovaries, so that the satisfactory end result does not justify the deliberate selection of this method of treatment for congenitally aplastic cases.

More extensive operations which involved the taking of strips of mucocutaneous and cutaneous tissue from the labia, vulva, and inner aspect of the thighs, introducing them into a canal previously made between the rectum and bladder, and packing them in position with gauze, was the second advance made in technique.

Beck² utilized these fundamental principles in developing the details of his operation as early as 1900. He made a transverse incision immediately above the symphysis pubis, which was carried downward between the peritoneum and bladder, hugging the bladder closely until the space between the bladder and rectum was reached. A counteropening from the perineum was then made to meet the passage already created, to establish a continuous canal from above the perineum to above the pubis, but without any opening into the peritoneal cavity. Two skin flaps were dissected from the thighs, their bases being represented by the labia and their length being sufficient to reach through the extent of the newly formed canal. These flaps were seized with forceps introduced from above, drawn through the canal and sutured at the upper end. The suprapubic wound was then closed. Bumm and Puppel both split the labia minora, and tried to create a vaginal lining with these mobilized tissues, but contracture followed.

Graves³ developed a much better method of transplanting flaps from the labia and thigh. After incising the occluded tissue at the vaginal orifice and separating the bladder and rectum, the two labia minora are dissected off from above downward in such a manner as to leave a pedicle sufficiently large to furnish good circulation. The two surfaces are then split apart so that two paddle-shaped flaps remain. Two similar flaps, which have their bases at the two lower corners of the artificial opening, are dissected from the inner side of the thigh. All four flaps are then sutured together over a glass form, after placing several catgut sutures with the ends left long in the vault of the artificial cavity. When the skin pouch has been nearly completed, the glass form is removed and the catgut sutures are brought out through the skin pouch. The pouch is then inverted and the sutures are tied so that the transplanted flaps fit snugly into the artificial cavity.

Mackenrodt⁴ suggested covering the surface of the newly opened vaginal canal by transplants of mucous membrane from another patient, but the futility of using isografts is now well recognized.

Sneguireff⁵ was apparently the first one to utilize a portion of the rectum for the formation of a new vagina. His operation consisted of making an incision along the border of the lower portion of the sacrum and coccyx, resecting the

of twelve. She had previously consulted five other physicians because of the amenorrhea; two of them had subjected her to anesthesia and some sort of a minor operative procedure, the nature of which could not be ascertained.

My purposes in making this presentation are: first, to record the operation in the literature under the names of its originators, so that Drs. Frank and Geist may receive the credit which is due them. The term "satchel-handle" operation is picturesque, but fails to identify

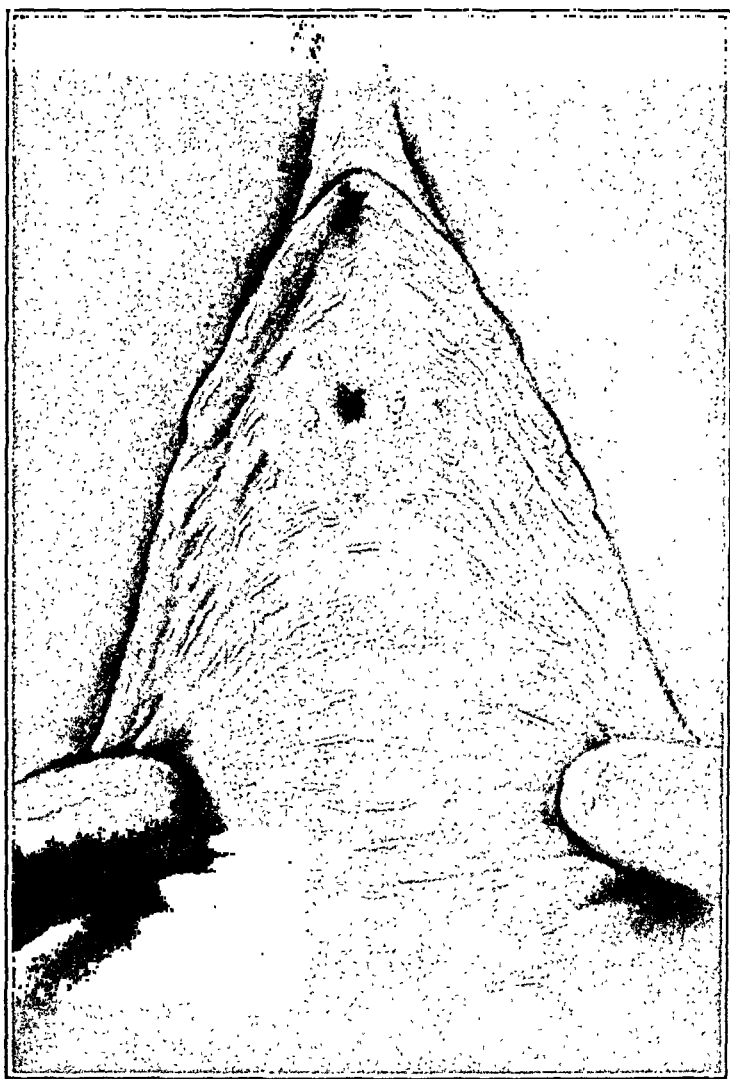


Fig. 1.—The usual appearance of the vulva in cases of congenital vaginal aplasia.

the technique with its proper name. Second, as the operation is now done, it differs slightly in detail from its original description. Third, the refinements of the daily treatment of the patient are of the utmost importance and may well be emphasized; and, fourth, a series of illustrations may clarify the technique for some one else who plans to do a Frank-Geist operation. I am indebted to Dr. Samuel H. Geist for his personal advice, which was courteously given from time to time as the several steps of the operation were carried out.

Although his ideas had been antedated by Menge, Schubert described an operation in 1911 and again in 1923 which consisted of resection of the lower segment of the rectum with its transplantation into the space created for a new vaginal canal and fixation of the lower end of the upper rectal segment to the ring of the anal sphincters. The chief disadvantage of this operation is its predisposition to local infection and sepsis and, like the Baldwin, its relatively high operative mortality. The Popow-Schubert operation consists of a retroperitoneal resection, appropriating the lower 12 cm. of the rectum for the vagina, and drawing down the upper part of the rectum through the sphincter muscles and attaching it to the anal skin.

In 1927 Frank and Geist¹² published their "satchel-handle" operation, so-called because of the construction of a pedicle tube graft from the inner aspect of the thigh to secure tissue for lining the new vaginal canal. They outlined their technique for the various surgical steps, and reported one case in which the operation had been performed with a satisfactory result. In a second publication in 1932 the same authors¹³ referred to their original patient and reported three additional cases. They have now done the operation nine times.¹⁴ In 1932 Grad¹⁵ described a modification of the Frank-Geist operation with its application to one patient. Instead of using a tube graft, Grad made a skin graft from the thigh measuring 17 cm. long and 12 cm. across, with two curves at the distal end; the incision is carried to the full depth of the skin and the flap is then undermined to the extent of about one inch; after it is undermined the skin is sutured back to its original position and several days later the original incision is reopened and the flap is undermined throughout its full length and breadth except at its base near the vulva. The further mobilized flap is again sutured back to its original position and allowed to heal. After all soreness has disappeared and the tissue regains its normal appearance, the entire skin flap is loosened except at its base. The vaginal tube is then constructed from the skin flap with its surface inside. This is tucked into the pelvis between the bladder and rectum. A few days later the skin flap is gradually severed from the vaginal orifice, the base of the flap replaced in its original position, and the rest of the granulating surface repaired with Thiersch grafts.

CASE REPORTS

The first of three patients, R. K., with congenital aplasia of the vagina (Fig. 1) came under my observation in 1928. She was an asthenic, unattractive female of thirty-four years, devoid of secondary sex characteristics and without interest in the opposite sex, although the urethra was greatly dilated. There was no indication for the correction of the developmental defect in this woman.

The second patient, R. F., aged twenty, with well-marked secondary sex characteristics and who was contemplating marriage, also presented herself in 1928 and was referred to Drs. Frank and Geist for operation. All experienced pelvic surgeons appreciate the difficulties involved in a secondary plastic operation, such as the repair of a vesicovaginal fistula or a third-degree perineal laceration, after previous attempts at correction have been made by inexperienced operators and resulted in failure. I therefore deemed it desirable to see the technique carried out in all its details, and to familiarize myself with the practical points in the daily care and treatment before undertaking one of these operations personally. Having had these advantages, I felt justified in assuming full responsibility for the third patient, who presented herself in 1936. This was a girl of nineteen, who had well-developed secondary sex characteristics, estrin in her blood, a strong sex urge, and was engaged to be married, although she had never menstruated. Abdominal cramps, backache, and headache had occurred at monthly intervals since the age

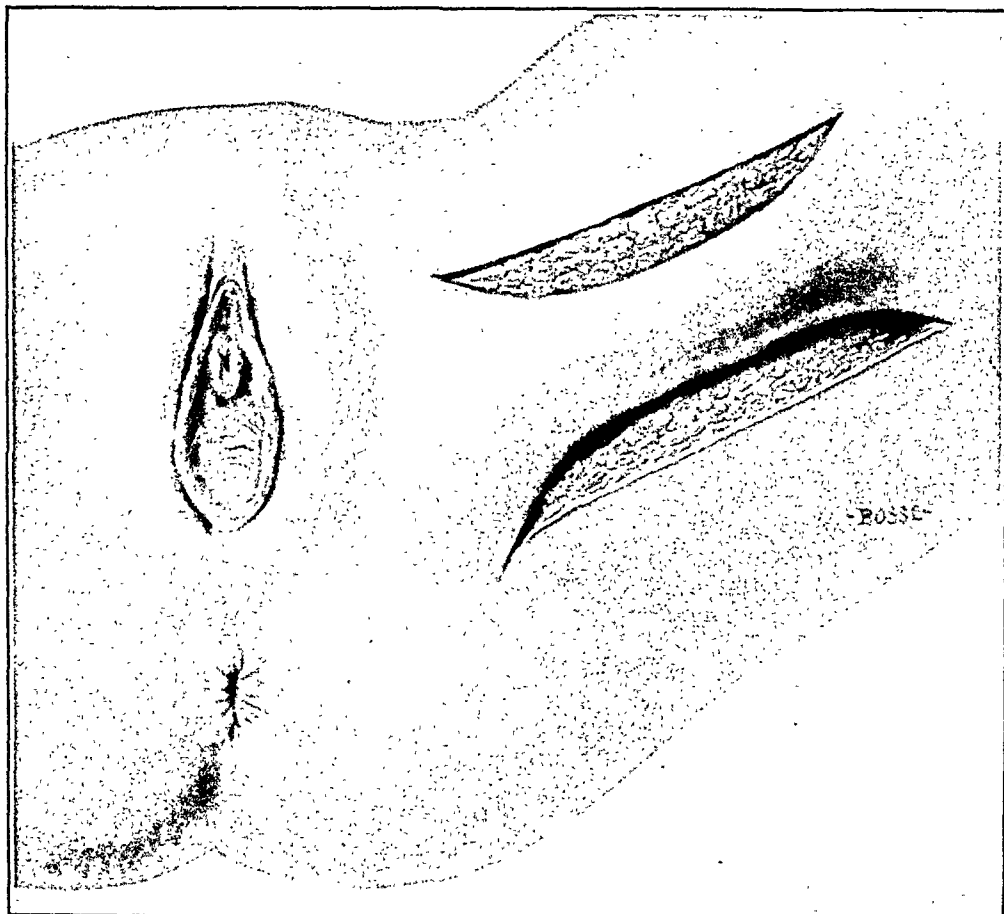


Fig. 3.—First step in the construction of the tube flap.

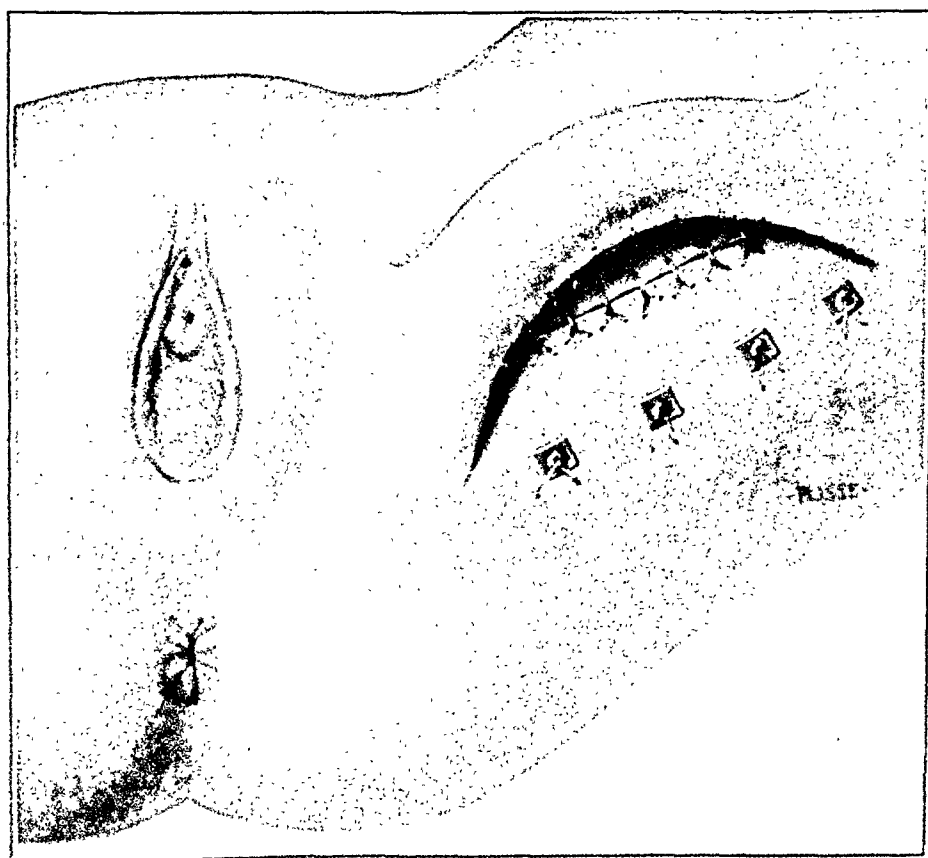


Fig. 4.—The margins of the flap have been united with interrupted silk sutures and the skin edges approximated beneath the tube.

PROCEDURE

The Frank-Geist technique includes three distinct operative steps, with occasional interspersed minor procedures, numerous dressings and meticulous attention to detail. The operative field should always be thoroughly scrubbed with green soap and water, but strong antiseptic solutions should be omitted. The first operation consists of making a skin flap on the inner aspect of the thigh six and one-half inches long and three inches wide (Fig. 2) and converting it into a pedicle tube. The parallel incisions are not carried down to the fascia lata, as originally suggested, but only sufficiently far to leave a small amount of subcutaneous fat on the undersurface of the flap. The pedicles are slightly flared at each end and care

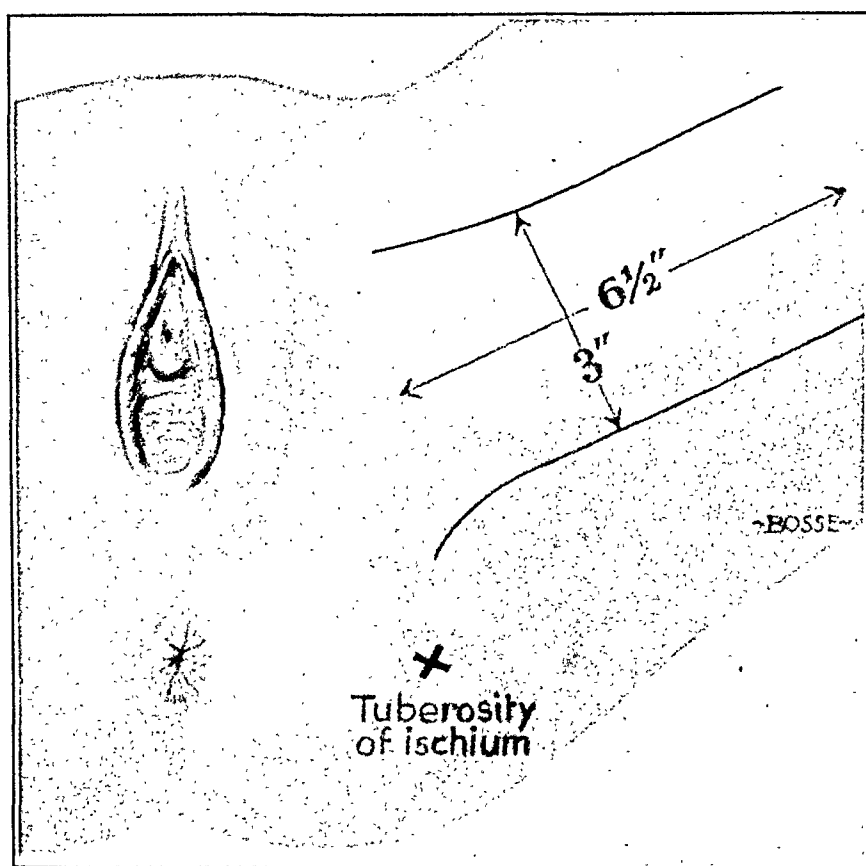


Fig. 2.—Outlining the margins of the skin flap on the inner aspect of the thigh.

must be exercised to avoid bringing the margins of the proximal pedicle too close to the tuberosity of the ischium, which might eventuate in a painful cicatrix on sitting, or too near the groin, which would limit the undermining of attached skin by the proximity of the dissection to the saphenous vessels (Fig. 3). After the fat left on the undersurface of the flap has been evenly trimmed, the tube is made by uniting the two cut edges with interrupted silk sutures. The skin of the thigh on each side is then undermined for an inch or two and, after delicately ligating all bleeding points, the mobilized skin edges are slid together beneath the tube and approximated with interrupted silk sutures. Three or four silkworm-gut retention sutures, secured at each end with small lead squares and perforated shot, serve to minimize the stress on the line of union (Fig. 4). A little fat is necessarily left exposed at the ends of the pedicle. A small sheet of rubber tissue in-

curved incisions which bring its base closer to the labia. It is then inverted so that the skin surface is inside and draped over a hard-rubber vaginal plug of appropriate size, through the top of which a small hole has been drilled (Fig. 9, *A*). The lateral margins of the flap are fastened together with three plain catgut sutures and, after proper disposition of the tissue over the plug so that the pressure is everywhere equalized, the apex of the transplant and the hole in the plug are transfixed with a long straight needle carrying a silk thread; one end of the thread is brought through the lumen of the plug, the other left on the outside of the flap, and the two ends tied at the margin of the plug, thus firmly fixing the apex of the flap (Fig. 9, *B*). The pedicle is rotated 180° toward the vaginal introitus and the

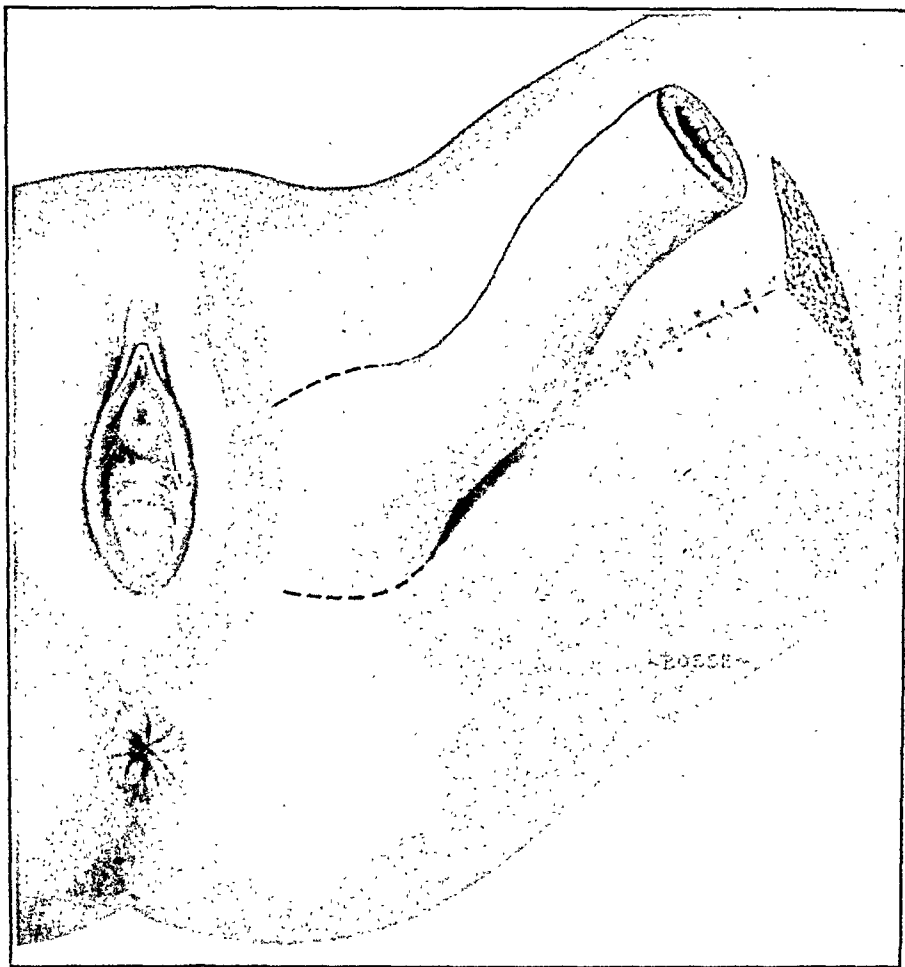


Fig. 6.—The distal flap attachment completely severed.

flap-covered plug inserted into the newly created vesicorectal space (Fig. 10). Three or four interrupted sutures fix the free end of the flap to the vaginal orifice. No attempt is made to repair the denuded area at the base of the lengthened flap. A Pezzer self-retaining catheter is introduced into the bladder and left for eight days. Continuous pressure on the vaginal plug is maintained by means of an overlying rubber sponge and a tight T binder. The diet is restricted to fluids. Small doses of paregoric are given for a day or two and the bowels are not allowed to move for eight days, although a rectal tube may be used to relieve accumulations of gas. The catheter is irrigated daily with warm boric acid solution. Discharge from the denuded area on the buttock, the vaginal canal, and the lumen of the plug may be

serted between the tube and underlying united skin edges separates the opposed lines of union and protects the raw areas. A gauze holster is placed on each side of the tube and the whole operative field covered with a light dressing. For several days the discharge from the exposed area is quite free, requiring frequent changes of dressings. The sutures are removed after ten days and a day or two later the patient is allowed up in a wheel chair. Daily dustings with thymol iodide help to keep the wound clean and dry. After three weeks the distal attachment of the tube flap is incised slightly on each side, under gas or local anesthesia. The detachment is carried further a few days later, thus leaving only a small area of attachment in the center (Fig. 5).

The second operation is done about four weeks after the first. The narrow remaining attachment of the distal extremity of the flap is completely severed

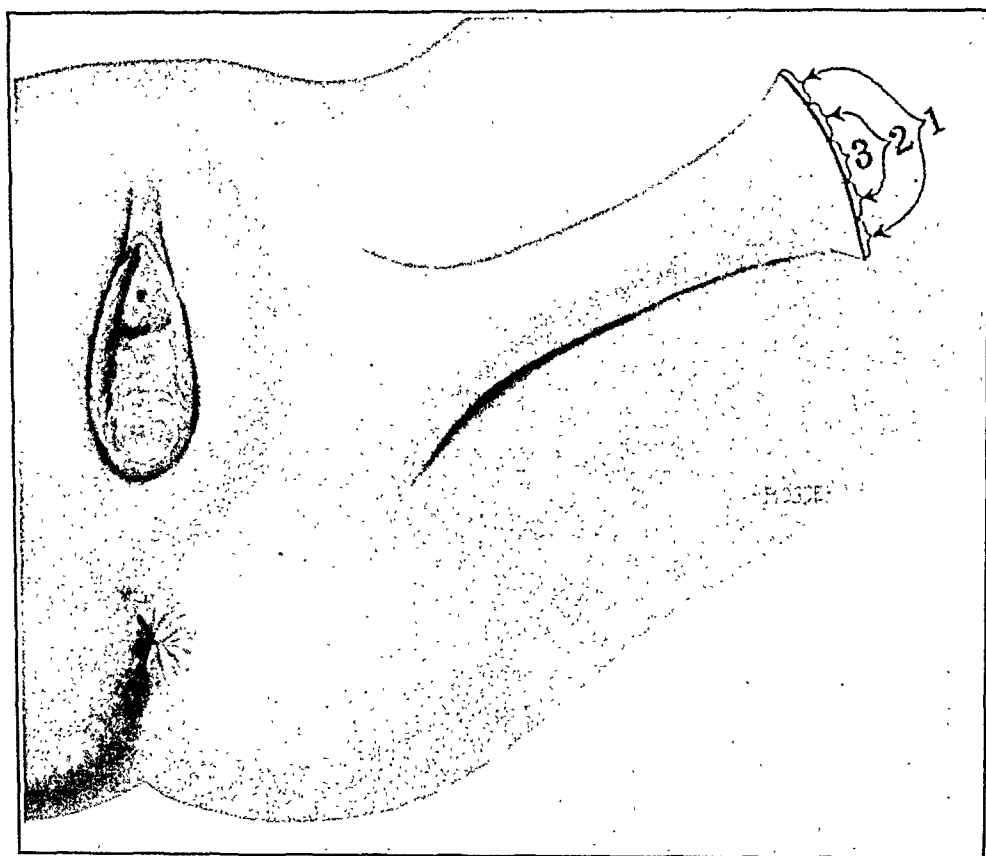


Fig. 5.—Showing the method of mobilizing the distal attachment of the tube flap by progressive incisions.

(Fig. 6) and the line of union on the undersurface of the tube reopened throughout its entire length. After trimming the scar tissue from the cut edges, the flap is temporarily wrapped in a large gauze pad, wrung out in hot saline solution. The tissue partition occluding the vaginal space is incised transversely (Fig. 7) and two of the operator's fingers are insinuated between the bladder and rectum up to the peritoneal reflection (Fig. 8). This blunt dissection is surprisingly easy, provided the proper line of cleavage has been entered. The incidental bleeding is quite free, however, because the vaginal venous plexus is necessarily traumatized and one or two ligatures may be required. The vaginal space is then stuffed with gauze until the preparation of the flap for insertion has been completed. The proximal attachment of the flap is still further mobilized and lengthened by two

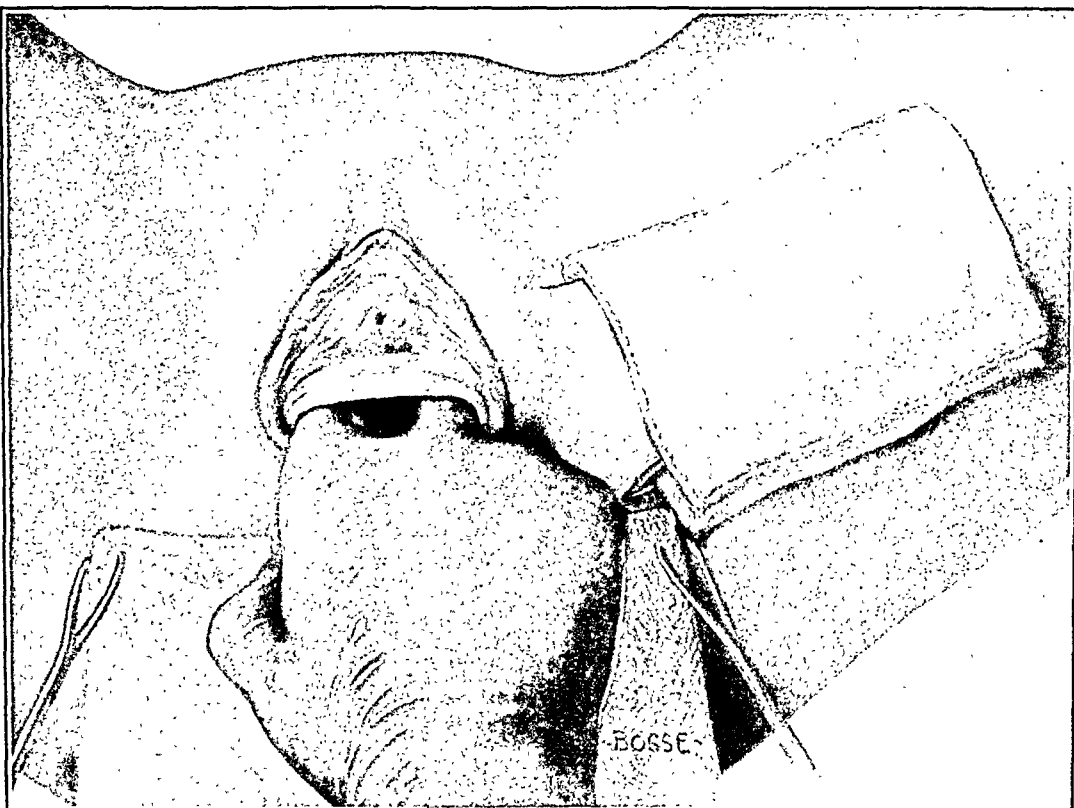


Fig. 8.—The flap is wrapped in a wet gauze pad while the vaginal dissection is carried out.

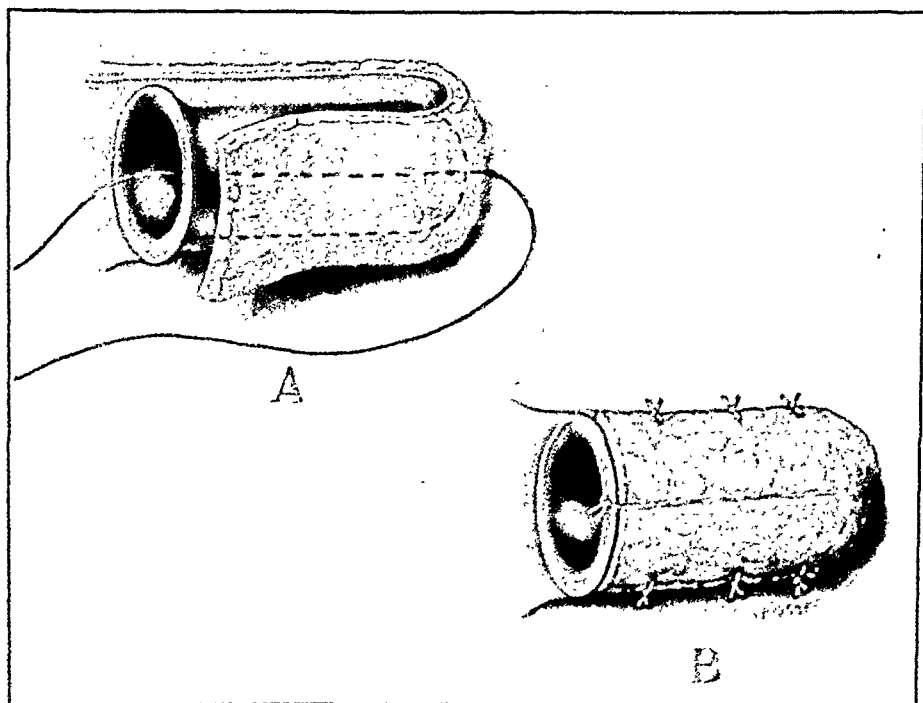


Fig. 9.—A, The flap is draped over a hard-rubber vaginal plug and fixed with a transfixion silk suture. B, The lateral margins of the flap are fastened with interrupted catgut sutures.

free and somewhat offensive for the first few days, but this is easily controlled with gentle potassium permanganate irrigations. Scrupulous cleanliness and frequent change of dressings are essential. After eight days the catheter is removed, the silk thread holding the flap on the plug is cut and withdrawn, and the bowels are allowed to move. At the end of two weeks the new lining of the vaginal canal is found tightly adherent to adjacent tissues, so that the vaginal plug can be removed and replaced at the patient's convenience. By the end of the third week, when the entire field is dry, the detachment of the flap from the covered margin of the vaginal canal can be started. It is severed little by little, as in the case of the distal extremity.

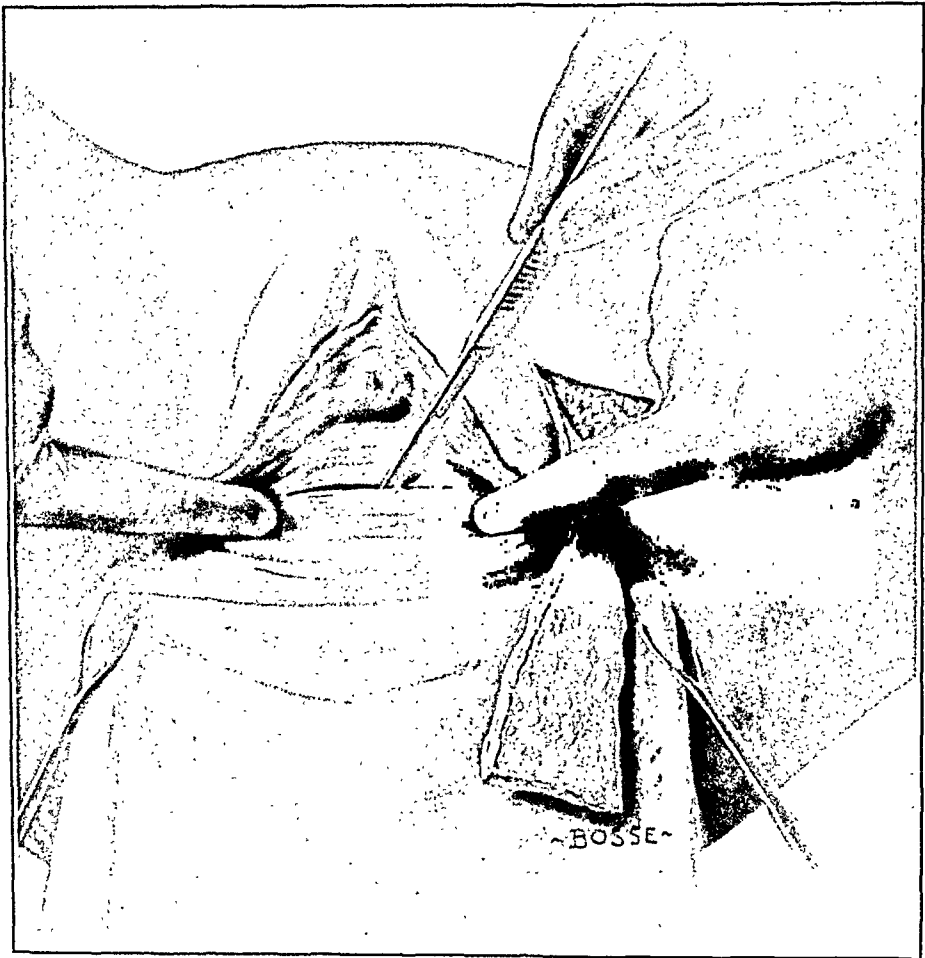


Fig. 7.—The tube flap opened and the incision through the occluding vaginal partition.

The third operation consists of completing the detachment of the flap at the vaginal orifice, freshening the granulating area and skin margins at the base of the flap, introducing a few more catgut sutures at the introitus and replacing the severed tongue of skin flap in the bed from which it originated (Fig. 11). It is wise to provide through and through drainage for a few days by means of a small rubber tube, to prevent the organization of a subcutaneous hematoma. Silk sutures are used for fixation of the replaced tissue. Although the patient can be discharged from the hospital two weeks later, the vaginal plug is, of course, worn continuously for several weeks thereafter.

The sooner the patient marries the better. Coitus is the best available method of dilatation to insure the patency of the new vaginal canal. A vaginal dilator should

that I might expect the development of a cystitis and pyelitis during this time, neither complication appeared. Perhaps the prophylactic use of hexamethylenamin and acid sodium phosphate prevented them. On the forty-sixth day, the sutures in the right margin of the vaginal canal were removed and the incisions in the proximal end of the flap started close to the vaginal orifice. The new vaginal canal easily accepted two fingers, and the flap was firmly united to the underlying tissues. A larger vaginal plug than the one previously used was inserted into the canal.

The proximal attachment was completely severed on the fifty-third day and sutured to the margin of the introitus, thus completing the lumen of the new vagina. The proximal pedicle was used to cover the granulating area from which the base of the flap had been taken. Despite careful hemostasis a small clot formed under this flap interfering with immediate union, so that it was necessary to dislodge the

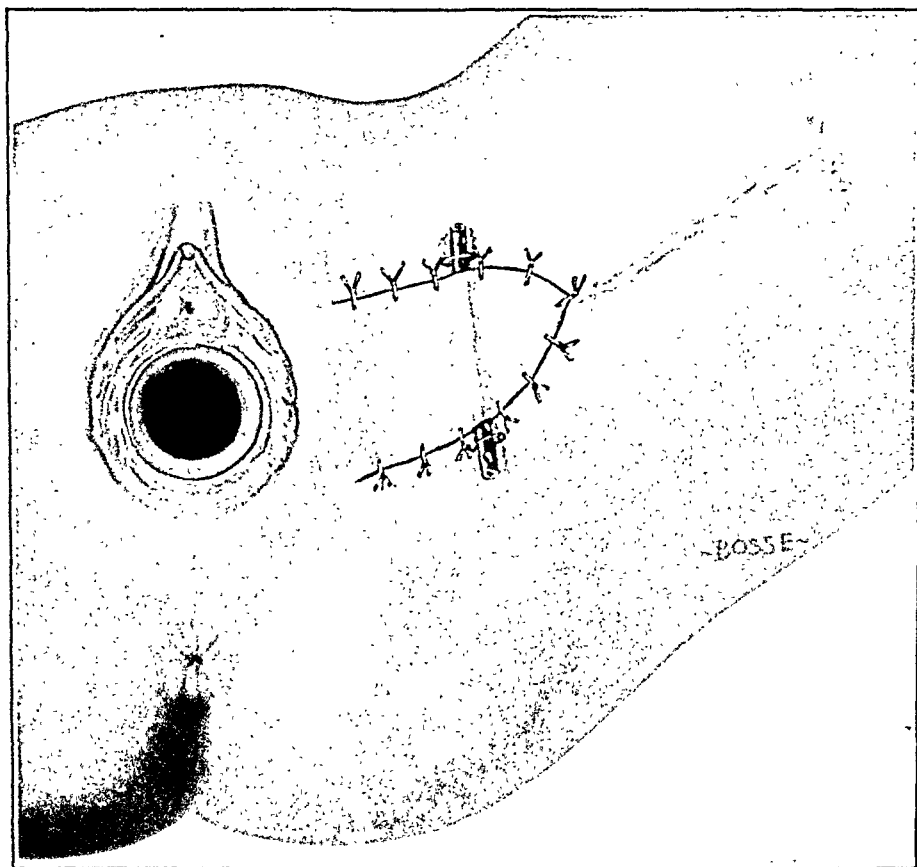


FIG. 11.—Resuture of the proximal pedicle of the skin flap back in its original position. The small rubber tube drain is good insurance against the formation of a subcutaneous hematoma.

clot by irrigation eight days later and insert a tiny through-and-through drainage tube. It would, therefore, seem wise to insert a similar tube at the time of the third stage operation to preclude such a clot organization. The patient was discharged from the hospital on the seventy-first day (ten weeks after admission) and instructed to wear the vaginal plug every night. She is now happily married.

The comparative utility of the four basic methods for colpoplastic construction may be briefly evaluated as shown in Table I.

The Frank-Geist operation confines the patient to the hospital for about ten weeks and imposes a responsibility on her as well as on the surgeon. The prolonged hospitalization and the constant cooperation

be passed every day during the next year to prevent contraction and, if the patient does not marry, the vaginal plug should be worn every night.

The patient on whom I operated was a very attractive, youthful-appearing, young woman with a typical feminine body contour, well-developed breasts, and pronounced secondary sex characteristics. With the patient in repose in lithotomy position, the vulva looked normal, but on separating the labia the external urinary meatus looked larger than normal and the vestibule below the lower margin of the meatus seemed unduly short. The fourchet appeared normal, but there was no evidence of a vaginal orifice or a hymen, the tissues being gradually fused by an occluding mucous membrane partition. This septum could be considerably indented with the tip of a probe.

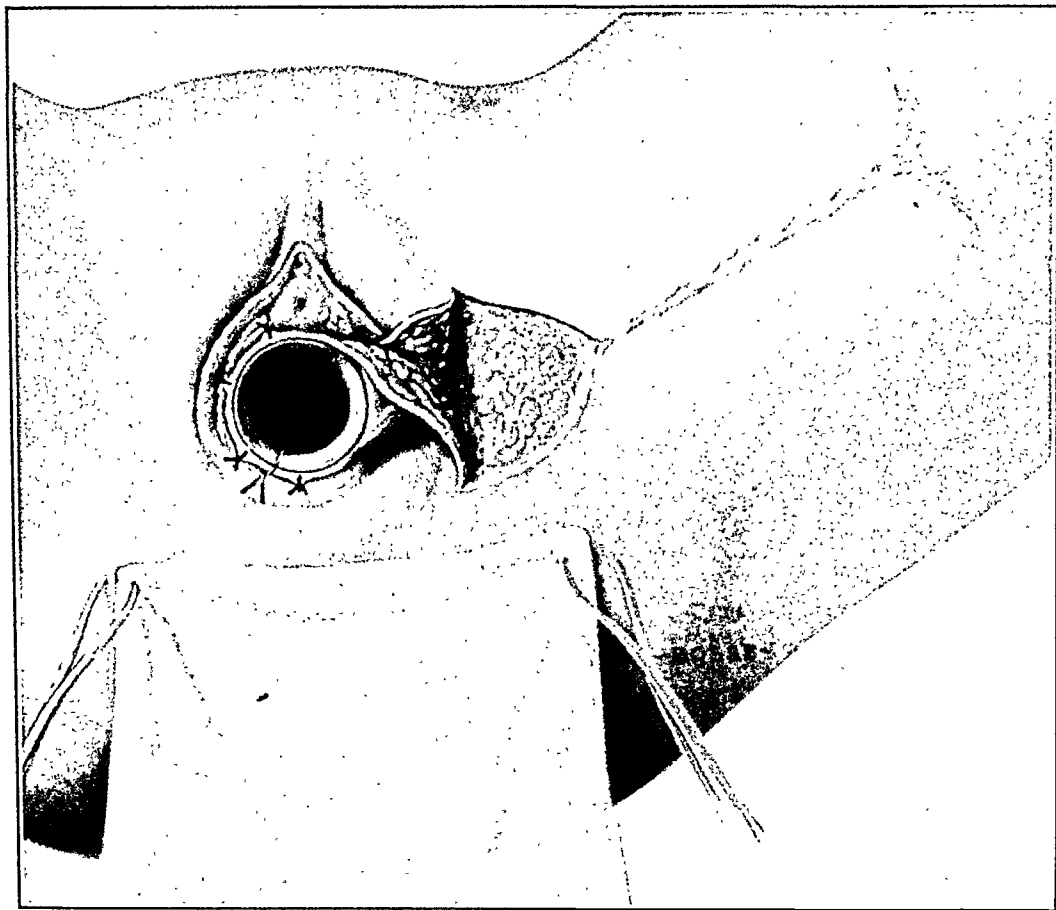


Fig. 10.—The flap-covered plug inserted into the rectovaginal space with a few sutures at the margin of the vaginal orifice.

The patient entered the New York Post-Graduate Hospital on Dec. 14, 1936, and the first stage operation was done the next day. The tube flap healed kindly, but a bacillus pyocyaneus infection appeared in the skin wound on the sixth day which interfered with primary union and delayed the incision of the distal end of the flap for several days. All sutures were removed on the fourteenth day. Incandescent light treatments were given daily until the twenty-first day when the small incisions at the distal extremity of the tube flap were started. Additional snips were made during the next week, the distal end being completely severed and the second stage operation performed on the twenty-eighth day. Immediately thereafter the bladder was drained with a self-retaining catheter and the bowels constipated with paregoric for eight days. Although Dr. Geist had cautioned me

Lately I have had a patient under supervision upon whom, I have done the operation that Dr. Dannreuther attributes to Graves. It involves the using of the labia minora to form the upper part of the vagina and two strips from the buttocks to form the posterior wall. This made a vagina but two inches deep and was not satisfactory.

Dr. M. N. Smith-Petersen found some time ago that Pyrex glass embedded in tissue caused a smooth glistening membrane to form around it and that the cavity contained fluid. From this he has gone on to construct cups that are placed between the head of the femur and the acetabulum in reconstructing hip joints that have been fused. On removal of the cup after a year he has found a smooth glistening membrane that contains clear fluid. Thus the hip joint is repaired.

It occurred to me that if the tissue between the rectum and the bladder, and the urethra and the retroperitoneal tissues could be easily separated, as they can be, in cases with congenital absence of the vagina, that it might be valuable to insert a Pyrex glass phallus and leave it for six months to a year to obtain a smooth cavity. At the end of that time the Graves method of grafting labia and skin up to the newly formed cavity would be used. In one case it was necessary to place the glass apparatus after the skin graft as it had already been done. So far it has been successful but there has been difficulty in holding the glass in place and preventing infection around it. I believe that by burying the glass in the soft tissues and leaving it there a successful cavity could be made and from it, after skin grafting of a minor degree, a satisfactory vagina.

DR. FRANCIS W. SOVAK, NEW YORK CITY (BY INVITATION).—In considering operations for the correction of congenital aplasia of the vagina, we have always been confronted with the problem: Do the end results justify the risk involved? The Baldwin and the Schubert operations carry with them the grave possibility of peritonitis or intestinal fistula and are only successful when performed by a very few expert operators. The Frank-Geist operation, however, apparently obviates these risks and insures a successful outcome when meticulous preoperative preparation, detailed attention to the various steps of the operation, and diligent postoperative care are carried out.

I am thoroughly in accord with Dr. Dannreuther's statement that no operation for the correction of aplasia of the vagina should be undertaken unless a woman has well-developed, secondary sex characteristics, evidence of estrin in the blood, a normal sex urge, and is contemplating marriage.

I would like to mention here what I believe to be a most important reason for performing these operations, and one, too often overlooked by surgeons who contemplate operations on the reproductive organs, namely the beneficial psychologic effect which the correction of such an anomaly has upon a woman who feels she is abnormal. Such a woman will readily submit to operation, and in fact will even plead for operative interference if she believes it will make her nearly as normal as her sisters. Unquestionably a woman who has been afforded a normal outlet for her sex drive, and also an opportunity for wifehood, will show a markedly uplifted mental attitude.

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—I have had within the last year two cases of congenital absence of the vagina, which after careful study of their endo-erines seemed to be fitted for reconstruction operation.

In regard to the technic, I am glad that it is not deemed necessary to take such a large pad of fat, because the thickness of this pad may interfere through pressure with the circulation of the skin. This was evidenced in one of my patients during the making of the tube flap so that I modified the operation by unfolding

TABLE I

OPERATION	ADVANTAGES	DISADVANTAGES
Baldwin	Flexible, elastic vaginal tube.	Intraperitoneal technic. High mortality rate. Profuse irritating mucous secretion.
Popow-Schubert	Retroperitoneal technic. Mucous membrane vaginal lining.	Varying degrees of rectal incontinence. Frequent intestinal fistulae. Occasional sepsis.
Graves	Extraperitoneal technic. Can be done in one stage. Short hospitalization.	Mutilation of vulva. In event of flap necrosis, there is no tissue available for second attempt. Possible growth of hair in vaginal canal. Subsequent scarring and contraction.
Frank-Geist	Extraperitoneal technic. No mortality. Well-mobilized flap, devoid of hair. If operation fails, tissue from opposite thigh is available.	Prolonged hospitalization.

which may tax her patience are just as essential as the faithful attention to detail by the operator. The chief advantages of the procedure are its assurance of a serviceable vagina and its freedom from mortality.

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DISCUSSION

DR. JOE V. MEIGS, BOSTON, MASS.—Dr. Dannreuther's advocacy of the use of plastic surgery from below instead of intestinal surgery from above is sensible. I believe that the use of a method that involves resection of any part of the intestine should only be undertaken by those surgeons who are doing considerable intestinal surgery, and not by those of us who are unused to it.

I should think by using one leg only, as Dr. Dannreuther has described the operation, it would be necessary to take too much skin from that one member. A few years ago Dr. Stephen Rushmore of Boston, in the September, 1929, number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, presented a method of similar type. He formed tube grafts on both legs, and then before inserting them split the grafts open and sutured them to one another and thus obtained a very good sized vaginal canal.

The operation is simple, the period of hospitalization lasts two to three weeks, and the surgical risk is practically zero when usual surgical precautions are used.

DR. W. WAYNE, BABCOCK, PHILADELPHIA, PA.—I did a similar operation to that mentioned by Dr. Counseller before the Clinical Congress of Surgeons held in Philadelphia last year. A thin quadrilateral skin graft was taken from the girl's thigh and sewed inside out with very fine wire over a test tube of appropriate size. This was introduced into a pocket readily formed between the rectum and bladder and the test tube held in place with wire sutures. At the end of about a week the test tube was withdrawn and the graft found to have entirely healed in place, leaving a canal lined with skin. The patient was discharged about a week later, with instructions to introduce daily a well-lubricated test tube of appropriate size. The result seems to be entirely satisfactory. The method is but a modification of the Esser inlay graft and a properly modeled stent of dental modeling compound may be used and buried by suture with the ensheathing graft for a week or ten days. I certainly can commend this operation as being very simple and very effective.

DR. DANNREUTHER (CLOSING).—I disagree with the statement that we see few of these cases of congenital absence of the vagina, but I can agree that we see very few that are suitable for operation. I have seen two additional patients since the one operated upon last year, but they were not interested in future marriage, had no secondary sex characteristics or estrin in the blood, and there was no indication for any type of surgical intervention.

The chief objection to the Graves operation is that the vulva is mutilated. I deem it advisable to preserve all of the attractive features of these young women. In the second place, the Graves operation utilizes a graft from both thighs which leaves no available tissue in the event of a failure, whereas in the case of the Frank-Geist operation it is still possible to reperform the operation by taking a flap from the remaining side.

Satisfactory heavy glass vaginal plugs in sets of six sizes can be secured from the Kny-Scheerer Company in New York. The rubber plug which is utilized in the Frank-Geist operation at first, for the purpose of transfixing the apex of the flap, is necessary because it is difficult to drill a hole through glass without breaking it. As soon as the flap becomes firmly adherent, glass plugs can be substituted. I think it is desirable to have the patient insert the plug every night, rather than to wear it continuously.

I also believe that it is wise to defer operation until just prior to the patient's marriage, because no artificial dilator will do what coitus can accomplish. When my patient was examined by my colleagues immediately after operation, they feared that the new canal would contract, but on reexamination four months after marriage they agreed that the vagina is now normal in its capacity.

the tube and sewing the flap back in its original bed. This modification worked very well, and when it was later placed in the space between the bladder and rectum, it was in a very healthy state.

My second case brought out a point which is very interesting in the light of what Dr. Meigs has said. The patient had had a former attempt in another city to reconstruct the vagina. Thiersch grafts had been used but the canal had contracted to an irregular channel not over 2 or 3 mm. in diameter. Two hours and forty minutes were consumed at one stage of my operation in removing scar tissue and dilating opening at canal. The usual tube flap was placed in the bed but on removing the plug later, practically the entire graft came out. She then wore a glass plug for several months and now has a perfectly normal vaginal canal more than 4 inches in depth. The question is, Did some of the Thiersch grafts remain, did some of my own tube graft remain, or by using the glass plug did this vaginal cavity develop a soft, glistening lining? What Dr. Meigs has said, together with this experience makes one wonder whether or not it is necessary to put the patient through the many and tedious stages of a tubular graft operation in order to create a vaginal canal.

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—Construction of a new vagina must be done by one of two procedures, either by using a portion of the intestinal tract or by using pedicle skin flaps. The Baldwin operation which utilizes the small intestine is not unusually difficult but is associated with a rather high mortality. If the mesentery of the ileum is short, as is often the case in congenital absence of the vagina, the ileum cannot be brought down into the vaginal position without considerable tension. If the mesentery is under tension the vessels will undergo thrombosis which will cause the implanted intestine to slough.

If pedicle flaps are used in the reconstruction, several operative procedures are necessary; these necessitate repeated and prolonged hospitalization. Unless one is particularly skilled in the use of pedicle grafts, failure is likely to ensue.

I would like to present a new operation for congenital absence of the vagina, which I have developed following the suggestion of Gilles and McIndoe of London. In this operation an inlaying graft is used. Their experience in constructing the external auditory canal, the nasal channel, and the male urethra by this same principle suggested the construction of an artificial vagina. The success in other conditions seems to be attributed to maintaining the channel by a tube or splint for four to six months until the period of contraction has passed, when the splint can be removed and the tract will remain in a normal state.

The procedure consists in obtaining the correct cleavage plane between the bladder and the rectum. Care should be used to keep adequately away from the urethra and bladder, which safeguards against injury of these structures. A rubber tube which conforms to the depth and diameter of the vagina is then selected. This tube is covered with a mastic solution for the purpose of holding the graft in position for ten to fourteen days. A split Thiersch graft which is large enough to cover the rubber tube is then obtained from the inner aspect of the thigh. This is carefully placed in the site of the new vagina and held in position by an obturator placed in the open end of the tube. The tube is removed on the tenth or twelfth day, at which time the new tract is completely covered with a thin layer of epithelium. The tract, which now resembles a normal vagina without a cervix, is cleansed with warm irrigating solution. The rubber tube at this time is replaced by a solid splint which completely distends the vagina. The splint, which is held in position by a sanitary belt, is worn constantly for four to six months and is removed by the patient once a day when the vagina is to be cleansed. After the contraction period has safely passed, the splint is removed and the vagina, which appears as a normal one, will remain as such.

operation with an attempt to restrict any consequent peritonitis to a limited area. To this end, the Hirst principle was adopted: i.e., the suture of the uterine to the contiguous parietal peritoneum around the projected uterine incision, in such a way as to eliminate the objectionable features of the Hirst operation, which are:

1. It is not applicable to the low type of section.
2. In order to provide room for the delivery of even a normal head, each side of the elliptical suture line must be at least 18 to 20 cm. long, otherwise the sutures are almost certain to tear out, defeating the purpose of the operation.
3. If effective, the uterus is left adherent over a great area high up against the anterior wall of the abdomen—more often, with involution and the continuous drag of the heavy uterus, the adhesions are likely to give way, again defeating the purpose of the operation.

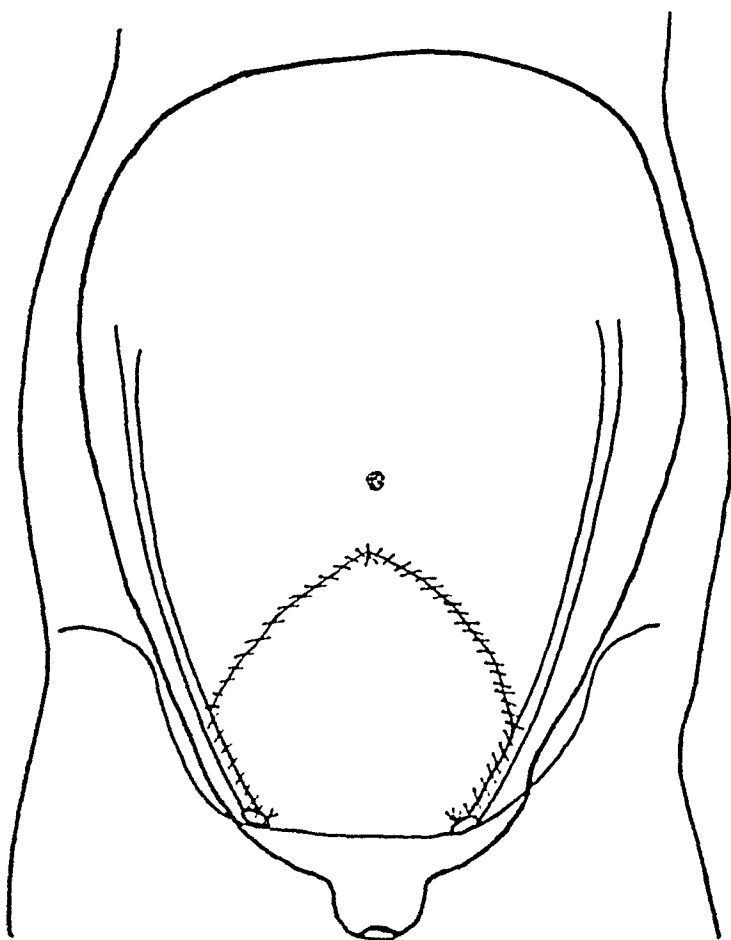


FIG. 1.

In order to eliminate these disadvantages, a line of continuous suture excluding the general peritoneal cavity from the field of operation is started at each internal inguinal ring: the round ligament is sutured to the parietal peritoneum to a level varying with the lie of the ligaments; from this level, the line of suture is carried obliquely upward and in-

CESAREAN SECTION IN INFECTED CASES*

WILLARD R. COOKE, B.A., M.D., GALVESTON, TEXAS

ONE of the all-too-familiar problems of obstetrics lies in the previously mishandled case in which cesarean section, contraindicated by infection, is the only alternative to a destructive operation upon a living fetus or a probably fatal attempt at its operative delivery. Each of the procedures which have been devised in the attempt to solve this problem (Porro, Küstner, Latzko, Hirst, Portes, pubiotomy with or without vaginal hysterotomy, etc.) has its peculiar difficulties, disadvantages, and dangers: which are so well known as to require no comment here. This paper is the account of another attempt to effect a solution of the problem.

Since peritonitis is by far the most frequent cause of death following section in infected cases, the first attempt was made in the direction of providing ample room for the delivery of a large fetus through a completely extraperitoneal operation. The greatest defect of previous extraperitoneal operations lies in the fact that the uterine incision, necessarily inadequate on account of the limited working space, may extend by tearing during the delivery of the head, with possible damage to large vessels, bladder, or ureter, or rupture of the peritoneum (which of course defeats the principal object of the operation). This first operation consisted of a modification of the Latzko principle: through a midline incision, the peritoneum was separated from the upper and posterior surfaces of the bladder and from the anterior wall of the uterus to the uterovesical reflection. Next, the anterior and posterior leaves of the broad ligaments were separated to a point above the uterovesical reflection on each side. This step permitted the making of a U-shaped incision in the uterus large enough to furnish an opening adequate to the delivery of the head without danger of tearing the peritoneum. The vertical wings of the incision lay a little mesial and anterior to the main ascending uterine vessels. While ample room is thus obtainable, the operation is difficult and tedious on account of the necessity for tying many transverse arteries and large veins as each vertical incision is made. The operation was performed only once, with no complications except a pelvic cellulitis with an abscess which required drainage by anterior colpotomy. The ultimate outcome of the case is not known, as the patient was not seen again after making an apparently complete immediate recovery.

As this first operation proved so formidable, and was not entirely free from the dangers inherent in other extraperitoneal operations, the second experiment was made in the direction of combining a transperitoneal

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and adnexa. Sixteen patients have had subsequent pregnancies: in 9 of these the indication for section was permanent, and subsequent ordinary sections were done (once in six cases; twice, with hysterectomy, in 3 cases); in 7 cases the indication for section was not permanent—delivery was effected in 6, the other being sectioned with hysterectomy for sterilization. Five patients had subsequent laparotomies (fibromyoma, cystadenoma, torsion, adnexitis, sterilization). In all of these note was made of the remarkable comparative absence of adhesions.

5. Is the operation justified by a reduction of mortality or of permanent morbidity in either mother or child? As noted above, peritonitis is the chief cause of death after section in infected cases. It was possible to obtain figures covering 16 similar cases in which ordinary section (classic only) had been performed by other operators. The contrast is evident in Table I. In the latter series peritonitis was the determining cause of death in the 12 fatal cases. Certainly, this operation brings about no reduction in morbidity or mortality from puerperal infection other than peritonitis; it is merely a matter of luck that the 15 grave and 9 moderate cases of metritis, cellulitis, thrombophlebitis, etc., escaped without mortality. As regards permanent maternal morbidity: there was only one case, and that of a minor nature, in the 23 traced cases (except, of course, certain morbidities due to the puerperal infection itself). For comparison, the results in 12 similar cases of many years ago, managed under the methods in vogue at the time, are presented in Table I. There is little doubt as to the effect of section on fetal mortality and morbidity—this is also evident from the comparisons in Table I.

TABLE I. RESULTS IN INFECTED CASES OF TYPES DESCRIBED, AS DELIVERED BY VARIOUS METHODS

	TOTAL CASES	MA- TERNAL DEATHS	MATERNAL MORBIDITY		FETAL MOR- TALITY	PERMANENT FETAL MORBIDITY
			IMME- DIATE	PERMA- NENT		
Section with exclu- sion	26	0	24	1	0	0
Section without ex- clusion	16	12	4	†	†	† (other operators)
Hirst	2	0	2	1	0	0
Latzko	4	0	4	1	1	0
Latzko, author's modification	1	0	1	0	0	0
Deliveries per vaginam:						
Destructive opera- tion on fetus	2	0	2	1	2	
High forceps	3	1	3	†	2	† (other operators)
Version and ex- traction	1	0	1	†	1	(other operators)
Pubiotomy	4	1	4	2	1	† (other operators)
Pubiotomy with hysterotomy	2	1	1	1	2	(other operators)

It should be definitely understood that this operation is not offered as an absolutely safe means of dealing with cases of the type mentioned: it is entirely possible that another series may show a high mortality.

ward across the anterior leaf of the broad ligament until the uterus is reached; thence to a point about 2 cm. above the top of the laparotomy incision, fixing the anterior wall of the uterus to the anterior parietal peritoneum. With the completion of both lines of suture, a Gothic arch is formed, each side and the base measuring about 17 cm., a total periphery of about 50 cm.; which is large enough to permit the delivery of almost any fetus without danger of tearing loose the lines of excluding suture. The highest part of the arch is only about 10 cm. above the pubis, and may be placed lower if a normal or small head is to be dealt with. A gauze pack is placed snugly against the lines of excluding suture, and a low type of section performed in the usual way. It has been found best to drain the excluded area by means of a roll of rubber dam, through a stab wound. There are several minor points of technic which have been found to be important:

1. If the parietal peritoneum is permitted to retract laterally during the placing of the excluding sutures, it may prove very difficult to approximate the edges of the peritoneum in the closure of the laparotomy wound. This retraction is prevented by holding the edges of the peritoneum with forceps until the excluding sutures are completed.

2. The first stitch at each inguinal ring must be so placed as to prevent leaving a loophole at this point—an accident which is very likely to occur if not guarded against.

3. The upper point of the arch of sutures must be at least $1\frac{1}{2}$ cm. above the upper end of the incision in the parietal peritoneum.

4. The stitches of the excluding sutures must be placed not more than 5 to 7 mm. apart.

Several theoretical objections to the operation are immediately apparent: these may be stated as questions, the answers consisting of such conclusions as we have been able to draw from the limited material.

1. Will the excluding suture and its consequent zone of adhesions be adequate to the restriction of a developing peritonitis to the excluded area? In none of the cases was there any suggestion of diffuse peritonitis, although definite peritonitis limited to the excluded area occurred in 21 of the 26 cases; in 3 suppuration continued after the healing of the stab wound, and in these the borders of the abscess followed sharply the Gothic arch of the excluding sutures.

2. Is involution interfered with by the abnormal location and fixation of the uterus? So far, there has been no evidence of subinvolution (except as is usual in puerperal infection), either immediate or delayed.

3. How long does the uterus remain fixed high in the abdomen? In all cases until after the active inflammation has completely subsided, a period occupying from a few days to eleven weeks in this series. The uterus was found to have returned to an apparently normal position: in 8 cases, one month after the subsidence of active inflammation; in 13 cases, two months; in 5 cases, three months.

4. Are there any sequelae attributable to the operation itself? Twenty-three cases have been followed to date. One patient complained of chronic pain in the left lower quadrant; laparotomy discovered massive adhesions involving sigmoid

TABLE I. TWENTY PORRO OPERATIONS WITHOUT MATERNAL MORTALITY

UNIT NO.	INDICATIONS	FEBRILE BEFORE OPERATION	HOURS		HOSP. DAYS	FEBRILE MORBIDITY		REMARKS
			IN LABOR	B. O. W. RUPT.		BRITISH	STRASSBURG	
42998	Face pre-entation	37.8	15	20	15	0	0	Attempted conversion and bag induction
58650	Uterine inertia	Potential	30	30	10	0	0	Artificial rupt. of B. O. W. Bag induction 4 hr. before operation
63389	Flat pelvis; brow	37.4	24	10	14	X	0	Upper respiratory infect.
65955	DDS, test of labor	Potential	14	24	14	X	X	P. O. bronchitis. Art. rupt. B. O. W. 24 hr. before
67221	Flat pelvis, previous section	Potential	12	20	14	0	0	2 vaginal examinations
70310	Central placenta previa	37.4	0	0	14	X	X	Marked blood loss
71616	Contracted pelvis	38.0	15	18	14	0	0	
	Partial rupture uterus							
80634	Marked disproportion	37.3	36	7	14	X	0	Numerous rectal and 1 vaginal examinations
88731	Flat pelvis, DDS	Potential	14	13½	46	X	X	
97180	Flat pelvis	Potential	16	14	21	X	X	Wound infection
99756	Breech, contracted pelvis	Potential	12	10	14	X	0	Feet in vagina, 3 hr. vag. exam. at home
99755	Placenta previa	Potential	0	18	14	0	0	Artif. rupt. B. O. W.
97181	Placenta previa and abruptio	38.0	16	14	21	X	X	Bag insertion 14 hr. before oper.
105360	Flat pelvis; test of labor	37.6	18	18	14	X	0	2 vaginal examinations
108673	Flat pelvis; test of labor	Potential	20	21	13	0	0	One vaginal examination
109552	Rachitic dwarf; previous section	Potential	0	14	12	0	0	Unsterile vaginal
115872	Abruptio placentae	Potential	6	0	12	X	X	Bag insertion 4 hr. prev.
117966	Cervical dystocia	37.4	52	35	15	X	X	3 vaginal examinations; peritonitis
119749	Cervical dystocia	Potential	48	24	11	0	0	2 vaginal examinations
120374	Uterine inertia	Potential	23	17	20	X	0	

Neither is this an operation for the occasional operator; to be performed with a maximum factor of safety, the excluding suture should be as carefully made as is necessary in extensive intestinal anastomosis.

2202 AVENUE M.

DISCUSSION

DR. P. BROOKE BLAND, PHILADELPHIA, PA.—In the first place most of us, I assume, look upon cesarean section as, technically, one of the easiest as well as one of the simplest major operations performed within the abdominal cavity. This simplicity, together with its drama or comedy, has led practitioners in general to become somewhat cesarean section minded. There is more levity with cheap stage play taken with cesarean section than any operation I know.

Though the practice is fairly common in many large institutions, it is far more frequent in the "small town hospitals" and in those with an "unbridled" staff. In institutions with "enforced" regulatory measures regarding staff privileges and conduct it is far less frequent. In my clinic as well as in many others throughout our land no member of the staff is permitted to perform a cesarean section without consultation with the supervising head or some other authoritative member of the department. This feature of departmental conduct should be made obligatory for staff membership, regular and courtesy, in every institution in this country.

Even in the most favorable concurrence of circumstances one encounters more complications, both immediate and remote, following cesarean section than almost any other abdominal operation. In my clinic the morbidity as well as the mortality is far higher than, for example, after a clean hysterectomy. Postoperative morbidity is always greater, and this implies that its sequel, mortality, must follow in a certain number of cases. Obviously, it is not possible to have the one without the other.

In the so-called clean or elective cases it is my custom to practice the classical procedure. I have been led to follow this course because in many instances my efforts to perform the low operation have been more or less frustrated, ending in a sort of surgical compromise, with part of the incision in the cervix or lower segment and part in the uterine body itself. In observing other workers perform the low section, I have on many occasions been impressed by the operation ending in precisely the same manner.

Heretofore, the numerous varieties of extraperitoneal and pseudoextraperitoneal methods have not made a compelling appeal to me. Since any plan or suggestion coming from Dr. Cooke is founded on practical experience, he almost persuades me to become an extraperitoneal cesarean sectionist, especially in cases of a suspicious character. However, in the frankly infected I believe the highest service is rendered by adopting a more radical plan, particularly if a patient has already one or more living children. In this group, following the delivery of the child, I extirpate the uterine body or remove the organ intact.

To leave a uterus literally sizzling with streptococci and at the same time discharging legions of these organisms into the blood stream seems to me wholly inadequate. In cases of this type it may be necessary at times, because of the mandate of a patient for future motherhood, to follow a less radical course, so here again one may apply the technic developed by Dr. Cooke.

DR. FRED L. ADAIR, CHICAGO, ILL.—Actual genital infection of the parturient woman has been considered a contraindication to any type of cesarean section except in case of the absolute indication when it should be associated with a

She was admitted with signs of severe sepsis after a neglected labor. Sometime after operation both abdominal and uterine incisions broke down in their entire length and pus was discharged freely from the uterus through the cervix and abdominal incision for nearly three weeks. The sterile hand introduced through the abdominal incision reached the posterior wall of the lower uterine segment. Her sepsis was so intense that the entire endometrium sloughed away and she has never menstruated since. Yet, during this time, she showed no signs of peritonitis and made a good recovery.

I have saved two severely neglected women by the Portes operation, one of whose endometrium also sloughed away and she ceased menstruating. With this procedure the pelvic organs may be preserved as they were in my two cases, or, if necessary, they may be sacrificed after the patient is out of her shock, really doing a Porro operation in two stages.

I have performed 68 peritoneal exclusion operations by means of sutures with gratifying results and would like to show the technic employed by means of four slides.

DR. S. A. COSGROVE, JERSEY CITY, N. J.—While it is undoubtedly true that procedures embodying the Hirst principle are simpler and quicker than true extraperitoneal operations, accidental tears of the peritoneum during their course do occur, and when so occurring are of much more serious import than when the same accident occurs incident to extraperitoneal section. I have made limited use of the Hirst principle, and concede its occasional feasibility under circumstances where low extraperitoneal section would be contraindicated, as perhaps in placenta previa. But, no matter what the difficulties and dangers alleged against extraperitoneal section, its increasing and successful use in the hands of a considerable group of surgeons must be a final and complete answer to allegations against it.

Jellinghaus revived interest in the Latzko section at the New York Lying-In Hospital in 1923. Kyle B. Steele reported from that institution in 1930 (*Am. J. Obst. & Gynec.* 19: 747) a series of 59 cases with a gross maternal mortality of five cases, or 8.5 per cent.

Henry T. Burns reported in 1934 (*Am. J. Obst. & Gynec.* 28: 552) a collected series of 79 cases, from 14 hospitals in the New York Metropolitan area, by fourteen different operators, with 2 maternal deaths, or 2.5 per cent, and with post-operative morbidity of only 52.6 per cent.

Albert H. Aldridge in 1937 (*Am. J. Obst. & Gynec.* 33: 788) reported a series of 27 cases from the Woman's Hospital in New York, with 1 death, 3.6 per cent. The average number of morbid days was 8.2, the average maximum postoperative temperature 102.6°F.

It is my privilege to report here, from the Margaret Hague Maternity Hospital, in a period of six years, 74 cases of Latzko extraperitoneal section, with 2 deaths, 2.7 per cent. Gross newborn and neonatal mortality, 7 cases, 9.4 per cent. Morbidity was 76 per cent; average number of morbid days, 5.1; average maximum fever, 102.6°F. There were ten different operators.

Dr. Steele in his article said, “. . . If it were feasible” spinal anesthesia “would be ideal” for this operation. This opinion we heartily concur in, and 68, or 92 per cent, of our cases were performed under spinal anesthesia.

Dr. E. G. Waters of our staff recently developed, without knowledge of its previous use, an approach to the uterus above the bladder, much like the old “Sellheim I” operation, but with a transverse section of the uterus. This procedure closely corresponds with Dr. Cooke's “modified Latzko” technic, but is simpler. Several of our recent cases have been done in this fashion, and Dr. Waters will subsequently report our experience with this technic.

hysterectomy or Porro operation. The absolute indication for cesarean section exists when it is not possible to deliver either a living or a dead baby through the parturient canal without serious damage or danger to the mother.

We recognize parturient cases with potential or actual genital infection. In the potential group we place those patients who have been exposed to genital infection by vaginal examination or manipulation during labor, those who have been in labor twenty-four hours or longer and those in whom the membranes have been ruptured twelve to twenty-four hours or longer. We do not perform any type of cesarean section on these patients if they can be delivered through the natural passages with relative safety to the mother and baby. Where the exposure has been considerable, a Porro hysterectomy may be a necessary sequence to an indicated cesarean section.

The actually infected patients include those who present clinical and laboratory evidence of an infection with or without localizing genital findings. In the latter group those without findings which locate an infection as extragenital are regarded as having a genital infection. Our opinion is that all actual infection is still a contraindication to cesarean section. The only indication for cesarean section in these cases is the absolute one, i.e., where a dead fetus cannot be delivered even by craniotomy through the parturient canal. When a cesarean section is necessary, we believe a hysterectomy is a necessary sequence.

With due respect for Dr. Cooke's opinion and recognition of his technical contribution to the performance of cesarean section which may increase the safety of the operation in properly selected cases, I must stand opposed to the adoption of the procedure proposed in infected cases except in those in whom there is an absolute indication for a cesarean section.

In such cases his operation may be as safe or safer than a Porro, though hysterectomy following cesarean section has in our clinic been followed by the results given below. We have records of 20 Porro operations in infected cases. Of these there were 12 potential and 8 actual infections. There were additional indications for hysterectomy in many of these patients. There was no mortality in our series (Table I).

I am sure a high mortality will follow in the wake of an extensive use of the operation described today in infected cases. I appreciate the fact that Dr. Cooke may have contributed a technic which will add to the safety of extraperitonealizing a cesarean section where it is absolutely indicated, but I am compelled to advise that its use be restricted to those unusual cases where the indication for cesarean section is absolute and in some of the patients who have potential but not actual infection.

DR. LOUIS E. PHANEUF, BOSTON, MASS.—Dr. Cooke has mentioned the Kroenig, Latzko, Hirst, Porro, and Portes operations. I have had experience with them all and feel that each has a place in the obstetrician's armamentarium. My own practice has been to employ the Kroenig type of operation, which I prefer to do with a transverse incision in the lower segment, for the ordinary type of case even after an efficient test of labor. For the woman who has had a long labor, ruptured membranes, vaginal examinations, and who shows some signs of exhaustion I have had recourse to the Hirst operation, referred to as peritoneal exclusion and which I have always performed by means of sutures. As to the Latzko operation, I have not convinced myself that this offered greater protection against peritonitis than does the Hirst procedure.

To show to what extent the Hirst peritoneal exclusion protects against peritonitis, I would cite the case of a young woman operated upon by this method in 1919.

each patient at the time of her prenatal visits. She was told that there might be a period of pain of many hours without progress. We also described the types of pain that might be present during this period and the symptoms of true labor. The results were most surprising. At the time of labor, patients discussed the symptoms they were experiencing and many times differentiated progress pains from preliminary pains. Rest periods were asked for instead of complete sedation. Later patients discussed their "preliminary period" of labor rather than "long labor" and "rest periods" rather than "painless labor."

Such observations interested me, but as yet my observations were only an impression. One thousand consecutive cases were studied, and our findings are presented as a basis for discussion.

A study of 1000 cases reveals the data as shown in Table I.

TABLE I

Preliminary Labor				
	TOTAL CASES	TOTAL NUMBER WITH PRELIMINARY LABOR	TOTAL NUMBER WITHOUT PRELIMINARY LABOR	AVERAGE DURATION PRELIMINARY WHEN PRESENT
Primiparae	539	375	164	15 hr. 51 min.
Multiparae	461	306	155	15 hr. 7 min.
Average Duration of Labor				
	FIRST STAGE	SECOND STAGE		THIRD STAGE
		WITH PRELIMINARY	WITHOUT PRELIMINARY	
Primiparae	9 hr.	2 hr.	2 hr.	9 min.
Multiparae	6 hr. 55 min.	48 min.	56 min.	8 min.
Interference				
PATIENTS WITH PRELIMINARY LABOR			PATIENTS WITHOUT PRELIMINARY LABOR	
177 or 17.7% in 1000 cases			70 or 7% in 1000 cases	

Three groups of patients were observed, those having true labors, those having false labors, and those having preliminary labors. Each group was classified from symptoms or events that suggested the nomenclature. In Group 1, true labors, there were 319 cases or 31.9 per cent.

SYMPTOMS AND EVENTS (GROUP 1)

1. The patient was sent into the hospital because of pain and other presumptive symptoms of labor.
2. The pains were progressively regular in time and in intensity.
3. There was early evidence of progressive changes in the cervix, notably softening, effacement, and dilatation, and changes in station.
4. Painless labors were seldom accomplished yet when sedatives were used cautiously and judiciously they were more effective in this period.
5. When a labor was well managed, the termination of labor was spontaneous or easy if interference was necessary.

In Group 2, false labors, there were 126 cases or 12.6 per cent.

We have then, in recent reports from a small area, 239 cases from 17 hospitals, in the hands of more than thirty operators, with a total mortality of 4.1 per cent, in a class of cases which constitutes *a priori* desperate operative risk. An operation which can yield this result cannot be passed over casually.

DR. COOKE (closing).—Disproportion on account of contracted pelvis was the indication in 16 cases. There was another group in which the fetus was too large for the normal or slightly contracted pelvis. The important group was composed of the patients in whom attempts to deliver were made before the patient was brought into the hospital with ruptured membranes, incompletely dilated cervix, etc. We consider such patients definitely infected.

I agree with Dr. Bland that cesarean section in infected cases is the most dangerous procedure in obstetrics. A survey in my own city showed that a group of operators had a mortality of 18.75 per cent in their general cesarean section work, and it is from this group that these twelve cases cited were derived.

Personally, I have always been afraid of cesarean section with hysterectomy. In a patient who has been in labor for a long time, it is dangerous to cut across the lower segment of the uterus or the cervix. The great gap so created, which is laden with bacteria, is left more or less open into the peritoneal cavity during the time required for hemostasis and peritonization. I have done this operation on more than one occasion; but I usually reserve it for the patient in whom a definite indication for sterilization exists.

THE PRELIMINARY STAGE OF LABOR*

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BY THE "preliminary period of labor," I designate all the presumptive symptoms of labor that may be present before there is evidence of progressive softening, effacement, and dilatation of the cervix. This term was suggested by the observation of patients sent into the hospital with pain that persisted for hours or even days without notable evidence of progress. From watching this group of patients, I was frequently in doubt as to whether a patient was in labor. Later, as I analyzed case records, I was impressed with two problems in the management of this period.

First: The influence the management of this period had on the succeeding stages of labor.

Second: The high instance of interference that seemed to have its incipency in this period.

The psychology of patients developed from hours of pain without progress was a problem of major importance. All patients had had prenatal care, and they were made familiar with the importance of cooperation during the prenatal period. In an attempt to control the psychology of patients during this preliminary period, full information was given to

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10. With each succeeding patient, we became more convinced that the management of this period determined later interference or a normal delivery.

11. Prenatal information to patients that they could have a normal spontaneous delivery and prenatal information to patients as to the importance of this period developed a cooperation that materially influenced interference.

12. The termination of this period is marked by progressive softening, effacement, and dilatation of the cervix. If the strength of the patient was maintained, the force and intensity of pains were conserved and dilatation was frequently very rapid.

These observations with this classification causes us to attempt to answer the question, when is a patient in true labor? We now would suggest that a patient is having true labor when there is progressive softening, effacement, and dilatation of the cervix with progressive descent. Furthermore, we would suggest that all the presumptive symptoms of labor that are present before there is evidence of progressive changes in the cervix and descent be known as the preliminary stage of labor.

This period may consume hours or even days. In one case alone it was one week from the onset of pain before the patient was delivered. Yet by maintaining the physiologic balance of the patient, it is interesting to note that the patient delivered normally with a pulse rate in the eighties. It is also interesting to relate that the duration of true labor was only seven hours. In this series it was not unusual to have a preliminary period of twenty-four to forty-eight hours followed by true labor of four to eight hours and a normal delivery.

The large number of cesarean sections reported for cervical obstruction has not been in keeping with my own experience. In our midwestern area we have found if patients have the right kind of contractions the cervix will dilate. Likewise, with few exceptions if patients have the right kind of contractions the baby will be pushed through the pelvis. This experience caused me to wonder if the preliminary period of labor might not be the explanation of the error of judgment in many cases when cesarean sections are done. With this thought in mind all the cesarean sections done in 17,000 cases were reviewed and only 3 cases were found in which a cesarean section was indicated. One was a cancer of the cervix, a second was a high cervical amputation without sterilization, and the third was a high cervical amputation with ventral fixation and without sterilization.

It would seem that 3 cesarean sections done for cervical obstruction in 17,000 deliveries would warrant the suggestion that cervical obstruction per se is a rare condition. It would seem that a better understanding of this period of hours of pain without progress might limit the number of cesarean sections done for cervical obstruction.

SYMPTOMS AND EVENTS (GROUP 2)

1. The patient was sent into the hospital because of pain and too often the pain was caused by the giving of castor oil.

2. The pain was characteristic since there was little or no evidence of progress.

3. There was little or no change to be found in the mechanism of labor.

4. In time all symptoms subsided from unknown causes or from the use of sedatives.

5. All patients were sent home and in time all returned to the hospital in true labor. In previous years bags had been used or the membranes ruptured to hasten true labor. We now believe that the onset of true labor is safer to the patient and that sending the patient home avoids interference.

In the preliminary group (Group 3) there were 681 cases or 68.1 per cent. It is this group that we would emphasize since the management of this period has had such a definite influence on the succeeding stages of labor.

SYMPTOMS AND EVENTS (GROUP 3)

1. Patients were sent into the hospital because of pain and other presumptive symptoms of labor.

2. Frequently the membranes had been ruptured for twenty-four or thirty-six hours before the onset of pain.

3. In this group almost every type of pain seen in labor was observed. The pains were regular or irregular, in time and in intensity, and were described by patients as painful, cramping, or pressure pains. Most characteristic was pain without progress.

4. Even after hours or days there would be little evidence of changes in the station or changes in the cervix.

5. Sedatives would modify the pain for a time, yet the pain persisted.

6. The persistency of the pain and the lack of progress made it impossible to send patients home.

7. Prenatal judgement that the patient could have her baby enabled us to wait complacently. Rupturing the membranes in selected cases seemed to have merit, but we were not convinced that it should be done routinely. However we were convinced that the use of bags is contra-indicated in this period.

8. In time there was definite progress in the mechanism of labor, especially descent and progressive changes in the cervix, notably softening, effacement, and dilatation.

9. If this period was well managed the onset of true labor was the same and the management the same as in Group 1.

that a more complete knowledge of the clinical course of labor and a better understanding of the significance of pain will go far toward lessening interference.

In the many years I have cared for women in labor my problem has been those patients with hours of pain without progress. My own mistakes of management and the high incidence of cesarean section and other forms of interference seen and being reported, cause me to suggest the preliminary period of labor as a part of the clinical course of labor.

1107 BRYANT BUILDING

WHAT IS MEANT BY THE TERM "TEST OF LABOR"?*

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CASES of pregnancy complicated by contracted pelves which are classified as "borderline" give us great concern as regards the proper method of delivery to be selected and it is in this group that the "test of labor" is frequently employed. Painstaking study, including pelvimetry, the x-ray, the use of various methods of impressing the head into the pelvis prior to labor, etc., may all leave us uncertain as to the ultimate outcome. The "test of labor" remains the final criterion, and upon its outcome we base our decision in favor of or against the performance of cesarean section. In obstetric literature, however, there is considerable lack of agreement as to the exact meaning of this term, which is reflected in our teaching, to the confusion of medical students and practitioners.

A consideration of the various definitions may be of interest. This is best done by reviewing the statements found in some of the many obstetric textbooks in use at present.

Burns,¹ speaking of pelves with conjugate vera from 7 to 9 cm. states: "The decision, whether the natural course should be awaited, or whether to interfere, and when and how this is best to be accomplished, is to be deduced not alone from the degree of the contraction. Equally should be considered, whether the head is large or small, whether its consistency is firm or compressible, whether it presents favorably, whether the action of the pains and of the abdominal pressure is regular and strong or not. All these cannot be observed and evaluated correctly before the rupture of the membranes. It follows therefore that in middle grade contractions nothing remains in the beginning of labor except to wait. . . . In the clinic the management of cases of moderate pelvic contraction turns out to be fairly

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In this series the question frequently arose as to what symptoms determine a test of labor. I recognize that this series is too small from which to make a positive statement, yet the suggestion that true labor is characterized by progressive softening, effacement, and dilatation of the cervix seems to be a noteworthy fact. At least it may serve as a basis for determining the type of pains necessary to dilate the cervix and push the baby through the pelvis.

SEDATION

The judicious use of morphine alone or combined with scopolamine has served me well in the management of this period. Complete sedation for hours of pain without progress has been most disappointing. I am led to believe that complete sedation is only possible with progressive softening, effacement, and dilatation of the cervix and then disappointing in many cases, if the interference rate is to be considered.

In this series there were 539 primiparae. Of this number, 164 had no preliminary period and 375 had an average preliminary period of fifteen hours and fifty-one minutes. The length of true labor of these with and without a preliminary period was eleven hours and nine minutes. There were 461 multiparae. Of this number 155 had no preliminary period while 306 had a preliminary period of fifteen hours seven minutes. The average duration of true labor of those having no preliminary period was seven hours fifty-nine minutes while those with a preliminary period had seven hours fifty-one minutes. The interesting problem was that both in the cases of primiparae and of multiparae where there was a preliminary period, it was slightly more than fifteen hours, which emphasizes the hours of pains that were present without progress. These facts suggest a different conception of the duration of labor and should be a means of differentiating those cases in which sedatives are most successful.

Another point of interest was that those patients having no preliminary period had an interference incidence of 7 per cent, while those with a preliminary period had an interference incidence of 17.7 per cent or a total of 24.7 per cent against a similar series that had an interference incidence of 47 per cent. This thought became the more impressive as patients were instructed prenatally what to anticipate when they were sent into the hospital. Equally impressive was the change in the attitude, toward the clinical course of labor, as members of the staff, internes and nurses developed this conception of hours of pain without progress.

It is very evident that interference is the fungus growth that is dwarfing our maternal and child welfare development. I do not believe our national superinterference has had a malicious environment; however there is sufficient evidence to warrant the suggestion that leaders in our specialty frequently do not appreciate the far-reaching effects of their influence. Too often well thought out procedures for definite groups become routines to the detriment of expectant mothers. It is my belief

Shears⁹ says that a test of labor should be given to patients with the conjugate vera between 7.4 cm. and the normal, but he does not define the term. "If at the end of two or three hours a careful examination shows that the head is still above the brim with no prospect of engagement, and confirms the fact that distinct pelvic narrowing exists, cesarean section or pubiotomy should be performed."

Cornell,¹⁰ in Davis' system, feels that "any patient whose labor is well established, who does not progress normally under proper narcosis, has been given a test of labor, regardless of the amount of dilatation of the cervix." He gives the average time for the test as twelve to eighteen hours, and says that it is not fair to the patient, the baby, or the obstetrician to allow a woman to remain in the first stage indefinitely.

Reed and Sabin,¹¹ in Curtis' system, recommended the policy of permitting labor to progress for a reasonable time, but do not mention "test of labor" or "trial labor."

Lavake¹² mentions the test of labor in borderline pelves, but does not define the term.

Harper¹³ counsels expectancy in "moderately contracted pelves": "Allow things to proceed as long as they are going along normally."

Wallich¹⁴ advises expectancy "to observe the effect of the natural forces, to allow, so to speak, the head to measure the pelvis." Failure of engagement is to be followed by symphysiotomy (in certain cases) or by cesarean section. No details of the test are given.

Tweedy, Wrench, and Solomons¹⁵ simply remark "cesarean section may appear the best method of delivery if there is great mobility and overriding of the head above the brim early in labor."

Eden and Holland¹⁶ do not mention the test of labor. DeSeigneux¹⁷ inclines to the view held by DeLee, Stander, and others; thus: "One cannot appreciate, before the rupture of the membranes, the possibility of the engagement of the head. The effort of the uterus acts directly upon the head only after the escape of the water, and it is only then that the head can mold itself sufficiently to pass, if that is possible, the contracted superior strait."

From the above it appears that obstetricians are not in accord in their conceptions of the test of labor and that the situation is further complicated by the use of the term "trial labor." Generally speaking, it seems that the term "trial labor," or "trial of labor," as at present employed, would best be defined as follows: the patient is allowed to go into labor spontaneously; after regular and fairly strong first stage pains are established, she is carefully observed for several hours, and the engagement or lack of engagement of the head is noted. The term "test of labor," as defined by some writers, means that the second stage has been reached, the membranes are ruptured, labor is allowed to proceed for two (or rarely more) hours, in order to see if molding and engagement might occur.

At this point, I wish to refer briefly to two papers detailing the results of tests (or trials) of labor in borderline contracted pelves. Others might be quoted, but these, one from the Red Cross Hospital of Lyon (France), and the other from the Johns Hopkins Hospital, can be considered as fairly representative of the conservative attitude. In

simple; first of all one must observe the effect of the expulsive efforts. If we realize that a spontaneous overcoming of the narrowing by the head is unlikely, so will the child be disengaged through a cesarean section above the pelvic ring, or room will be provided through the opening of the pelvic ring—pubiotomy." It can be seen that Bumm considers the rupture of the membranes to be an important factor; however, he makes no statement as to the degree of cervical dilatation.

DeLee,² while not formulating a definition of the term, advises that labor be allowed to proceed to full dilatation of the cervix, with avoidance (if possible) of premature rupture of the membranes; after the beginning of the second stage, the patient is observed in order to see what molding may accomplish, but a second stage test of two hours is considered sufficient.

Stander,³ in his revision of Williams' textbook, draws a distinction between a "trial labor" and a "test of labor." Thus: "By 'trial labor,' we mean, in general, from four to six hours of fairly active labor, the pains coming every ten minutes, lasting for forty to sixty seconds, and being fairly strong in character. . . . 'Trial labor' must not be confused with a true 'test of labor,' by which is understood a labor up to the point of full dilatation of the cervix for a period of two hours or longer with the membranes ruptured." He states that very few of his patients with contracted pelvis are subjected to the test of labor, a trial labor usually enabling him to foretell whether or not pelvic delivery will be feasible. He states, however, that engagement and molding occur only after the resort to the test of labor.

Irving⁴ states: "No set rules can be laid down for the conduct of a test of labor, and each case must be decided on its merits. The test may last from a few hours to forty-eight hours or more, and may in rare instances even include two hours in the second stage of labor. Our policy has been to perform cesarean section if no progress has been made after a reasonable number of hours of hard labor." It will be noted that in most cases, he confines the test to the first stage of labor.

Titus,⁵ in writing of the management of the relative and borderline types, says: "Cesarean section will be undertaken if a few hours of vigorous first stage pains fail to develop at least some evidence that the head may engage." Later, he refers to "not merely a test but a trial of labor," in patients for whom hospitalization is impossible. It will be seen that his conception of the terms differs from that of Stander.

Beck's⁶ opinion is in accord with that of Stander. He states that a real "test of labor" consists of at least several hours of active labor after the beginning of the second stage. Should engagement fail to occur, craniotomy is the safest procedure, though the low or the Porro section might be used, according to the conditions present. In cases of a diagonal conjugate of 10.5 to 11.5 cm., he prefers the "test of labor," whereas in patients with diagonal conjugates of 9.5 to 10.5 cm. he employed the "trial of labor."

Bland⁷ says: "With moderate overlapping of the head the patient may be given, under every possible aseptic safeguard, the test of labor; but if after a trial of six or eight hours of hard firm contractions no progress is evident, delivery may be effected by a low cesarean section." Note that there is no reference to the condition of the membranes or of the cervix; the only criterion stated is that of six to eight hours of hard firm contractions.

Vaux,⁸ in his revision of Edgar's textbook states: "If after several hours of second stage contractions the head has shown no tendency to engage and descend some, the likelihood of spontaneous delivery or of delivery by forceps or version is quite out of the question."

would be offset by the lessening of the maternal risk as compared to the risk of the severer test, and by the much more favorable outcome as regards the infants. I feel that the conception proposed is really the one which is entertained by most obstetricians, and that the situation would be clarified by the universal adoption of some such formula.

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931 CANAL STREET.

DISCUSSION ON THE PAPERS OF DRS. HAMILTON AND KING

DR. CHARLES W. MUELLER, BROOKLYN, N. Y. (By Invitation).—It is my opinion that this preliminary stage, as described by Dr. Hamilton, does actually exist. With the same premise in mind I have reviewed a series of 500 cases from the King's County Hospital of Brooklyn. Due to the short period of available time my results cannot be compared with the painstaking details presented by Dr. Hamilton but a few of my conclusions may be of interest.

We believe that less than 68 per cent of patients have this preliminary stage of labor. Also it appears that the duration of this stage is much less than fifteen hours or his average.

A large percentage of our patients are of Jewish and Italian descent. Their emotional traits may lead to a misinterpretation of the exact time of the onset, as well as the severity of their labor pains. Furthermore, in a hospital where the clinic patients are aware that their care is to be free, admissions occur for little or no pain. For these reasons our percentage of preliminary labor and of false labors should be high. Yet, I am sure that 12.6 per cent of our cases could not be classified as false labors. In my private practice false labor is relatively rare.

We have encountered a fair number of cases in which labor became established with a definite effacement as well as dilatation of the cervix and even with some descent of the presenting part, but in which progress would then be arrested for a number of hours. This might be termed an arrested first stage. Usually termination of labor is successful without interference in these cases.

each series, extreme conservatism prevailed, and the results would appear to indicate that this attitude is reflected in each series in a high fetal death rate.

Peckham and Kuder,¹⁸ reporting on 422 cases in Johns Hopkins Hospital in which the test of labor lasted thirty hours or more, found a gross fetal mortality rate of 19.23 per cent; a corrected fetal mortality rate of 13.56 per cent, a gross maternal mortality rate of 1.36 per cent, and a corrected rate of 0.91 per cent. Rhenther, Bucher, and Chartel,¹⁹ in 141 cases of slightly contracted pelvis (bassins limites), reported the results after the test of labor (*l'épreuve de travail*), with a "careful and sufficiently prolonged observation after the rupture of the membranes." There were three maternal deaths; one from toxemia, one from septicemia after low cesarean section, and one from "obstetric shock." One hundred thirty-four of the 141 were delivered vaginally, 7 were subjected to low cesarean section. Twenty babies were lost, giving a fetal mortality of 14.2 per cent. The authors conclude that better results were obtained by the employment of the induction of premature labor; in 100 cases thus treated the maternal mortality was 0 and the fetal mortality 13 per cent.

Based upon this review of the varying and more or less conflicting views of the authors quoted and upon a consideration of what really appears to be the course that the majority of obstetricians actually adopt, I would suggest that the following would be a proper conception of the test of labor. It would appear wise to eliminate the terms "trial of labor" and "trial labor" entirely.

In a pregnant primiparous woman with a borderline contracted pelvis (c.v. of 7 to 8 cm. in a flat pelvis or 7.5 to 9 cm. in a generally contracted pelvis) spontaneous labor is allowed to establish itself (the head is not engaged). After regular and fairly strong pains are established, occurring every five to ten minutes and lasting thirty to sixty seconds, labor is allowed to proceed for from four to eight hours, during which time the fetal heart tones are carefully watched. Some form of analgesia is advisable. The position of the head is noted by abdominal palpation, which may be checked by two or three (not more) rectal or very aseptic vaginal examinations. Should definite engagement occur, the feasibility of vaginal delivery is established. Should engagement not occur, or should the heart tones show fetal embarrassment, cesarean section, preferably of the low type, is to be performed.

To this conception, two objections might be raised. First, it is held by some that molding and engagement of the head in such a pelvis cannot occur until the second stage is established. With this idea I am not in complete accord; it is correct as regards the severer grades of disproportion, but not so far as the milder varieties are concerned. When it does occur, in cases falling in the first group, after what may be called the "true test of labor," a prolonged and difficult second stage is the rule, with a tedious forceps delivery and high fetal morbidity and mortality rates. The other possible objection would be that the cesarean section rate in the borderline group would be raised. If so, this

of the ischium. If we want to find out whether this head can go through we want to know first whether it will become fixed and secondly if it will become engaged.

For twenty years I have used three terms in determining the test of labor: first, the "trial of fixation"; second, the "trial of engagement"; and finally, the "trial of labor." This last I accept as being a complete effacement and a complete dilatation, and rupture of the membranes, followed by a few hours of good second stage labor.

The decision as to procedure must often be made earlier than the final trial of labor because a long labor, of more than six hours, is a dangerous thing if cesarean section be contemplated. The borderline cases with contracted pelvis are given the trial of fixation. Now the head does not necessarily have to be fully engaged for us to say this patient will come through, but if a patient will fix the head she will usually engage it, and if the head becomes really engaged it will usually deliver. By carefully observing the possibilities of fixation and engagement, one may often determine the possibilities of birth without subjecting the patient to the final test of labor.

It has been my observation that the preliminary stage of labor is almost never without some evidence of progress. I have had many of these cases of patients that Dr. Hamilton has discussed today, have had them go home after these distressing few hours of labor, and almost never have they come back without showing that progress was made. There is always some degree of effacement, sometimes a considerable degree of dilatation, although that is not so common.

DR. RUDOLPH W. HOLMES, CHICAGO, ILL.—I would regard true labor as starting only when the cervix gives evidence of structural changes, namely, softening and beginning dilatation. We must not confuse those weak, irregular contractions which precede true labor, and called by older writers *dolores praesagientes*, with true contractions of labor. The former are peculiarly phenomena of multiparous labors.

A true test of labor has been given only when the woman is permitted to progress until dilatation has been accomplished, and the membranes have been ruptured two hours. It is only when these two elements are accomplished facts that the head may descend when there is some cephalopelvic disproportion.

It is not the duration of labor which determines whether a secondary section may be performed. The vital factor depends upon what errors of omission or commission have been perpetrated during the hours of the test. I hold that there should not be any vaginal examinations during this test. No rectals should be employed until a definite indication for their employment arises. Pulse and temperature of the mother, auscultation of the fetal heart must be recorded every two hours, finally at half hourly intervals, even more frequently towards the last. During the early hours of the test the mother should be given regularly some hot gruel, soup, etc., but not milk, for the curds from the latter may be a distinct inconvenience if emesis occurs. The nurses and internes must be warned that the patient is a special risk and requires very special watchfulness.

DR. A. K. PAINE, BOSTON, MASS.—At the Booth Hospital, where we have a relatively large percentage of primiparous deliveries, we have adopted the rule that complete dilatation of the cervix must occur before the performance of a cesarean section in any relative disproportion case. Since adopting full dilatation of the cervix as indicative of an adequate test of labor, our cesarean section incidence, in the disproportion group, has dropped from 8 per cent to approximately 2.5 per cent. As for mortality, cesarean sections done after the patient has been in labor for some time represent our best group at the present time. Unexpectedly it has

I had hoped that the essayist would present a theory of the cause of onset of labor. This might explain why some patients have a preliminary stage while others have such an active, short, normal labor. Would a peculiar endocrine status explain this? If the onset of labor were due to the increase or decrease of some endocrine secretion, would not a lessened stimulus produce our so-called preliminary stage?

DR. H. L. GAINNEY, KANSAS CITY, KANSAS.—In the Kansas City District, I know of two hospitals with incidences of 32 per cent cesarean section in one and 14.7 per cent in another. In the latter I had an opportunity to review the cases and was able to class at least 75 per cent of them as cases of so-called preliminary labor. Cesarean sections were done by general men, the patients having been in labor for ten to eighteen hours without progress. Contraction of the pelvis was obviously not a factor. We noted in every case definite softening of the cervix and in most cases a descent of the head which would certainly mean that there was progress if not actual dilatation of the cervix. If this new term offers no more than the opportunity to bring about a discussion of the normal cause of labor among general practitioners it justifies itself.

DR. A. N. CREADICK, NEW HAVEN, CONN. (By Invitation).—In those institutions with adequate x-ray facilities pelvic mensuration and fetal measurements have greatly facilitated accurate observation. I still wait to take an x-ray until at or near term. The disadvantage of increased bulk and interposed fetal small parts is outweighed by the advantage of seeing the relation of that particular fetal head to that particular pelvic canal. It is difficult to estimate the dystocia due to increased pelvic inclination. The diameters of the fetal head may be measured by x-ray but the advantages to be secured by molding are not evident. Synclitism likewise cannot be measured.

The chief variable factors that remain are the voluntary and involuntary expulsive forces. It seems to me that this discussion can begin with such suggestions as these: (1) The term trial labor must be understood. (2) A careful analysis of the relation of presenting part and pelvic canal is essential. (3) No real disproportion being apparent, adequate contractions may be permitted. (4) No real trial is effective until the cervix is completely dilated. (5) Final dependence is put on vital signs of mother and fetus.

The chief disturbing factors to such a program are: (1) Pressure by the laity for a more active attitude. (2) Facility of performance of cesarean section. (3) Relative safety of cesarean section when done early, without too long an interval between rupture of membranes and time of operation, and when done without vaginal examination. (4) Certain occipitoposterior presentations causing edema and thickening of the cervix instead of its effacement. (5) The seriousness of any operative delivery where delayed until heart sounds show distress or maternal signs betoken exhaustion.

In the clinic at Yale, both in ward and in the private cases, induction during the thirty-six to forty weeks is practically abandoned. The incidence of operative delivery is rising. The duration of time allowed for trial labor is materially shortened. The old teaching of Williams of "Two hours of adequate contractions after complete dilatation" is outmoded.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—Twenty years ago I abandoned the term "test of labor" in borderline contracted pelves. However, we do have to give a test. Remembering the mechanism of labor, a test may be applied as labor does or does not progress through the various steps of the mechanism of labor. The first thing that happens is fixation of the head, and the next is engagement of the head. Engagement is now defined as the descent of the presenting part to the spines

difficult to explain to the general practitioner and occasional accoucheur that the progress of labor may be normal in cases having contractions forty-eight to seventy-two hours with little or no progress. There is very little attention given to this point in the average textbook.

DR. L. A. CALKINS, KANSAS CITY, MO.—While Dr. Hamilton's work has been going on in Kansas City, we have checked his results in other hospitals of the city. We feel that, while his percentage of preliminary labors is too high, we all have seen a considerable number. We have found that it is of definite help to keep this idea before our students. Dr. Hamilton stresses the particular importance of this concept to the patient. We agree with this, but of the greatest importance is the improvement in the psychology of the doctor involved in such a concept.

DR. HAMILTON (closing).—It is possible that my enthusiasm may have influenced statistics. Nevertheless in each case a record was kept of the preliminary stage as well as the first, second, and third stages. We have attempted to differentiate true labor, false labor, and this period of pain without progress which we have called the preliminary stage of labor.

The large number of cesarean sections done for cervical dystocia again causes me to suggest the necessity of differentiating types of so-called labor. Again, may I suggest that the hours of pain without progress, form a definite part of labor and must be treated as such.

DR. KING (closing).—The main point that I wish to stress against the teaching that a test of labor requires full dilatation is that such a procedure is associated with a high mortality. Figures from Johns Hopkins show a 19 per cent fetal mortality when the extreme test of labor was allowed. In that series about 1 per cent of the maternal mortality was charged to the complications resulting from a long test of labor. If we adhere to the definition of full dilatation and ruptured membranes, are we not going to lose more of the mothers and babies than if we adopted a slightly different conception?

In this compromise test there should be evident a thinning out of the cervix, some effacement, some sign of progress if there is going to be a fairly easy delivery. After four to eight hours of real labor, if the head is still floating above the pelvic brim, with no fixation and no engagement, then it is time for cesarean section.

also been our experience that the patients on whom we do transverse cervical operations, after full dilatation of the cervix, have relatively a more satisfactory convalescence. Obviously the low section is technically an easier operation when the lower segment is effaced and the cervix fully dilated.

Unfortunately, in 8 or 10 per cent of these disproportion cases, complete dilatation of the cervix will not occur within a reasonable length of time. We have set twenty-four hours as an approximate limit of the time we would ordinarily wait for complete dilatation. This twenty-four hours refers only to actual labor as shown by its definite effect on the cervix.

Fewer cesarean sections will be done if we allow each of these relative disproportion cases to have an adequate test of labor. An adequate test in our experience is complete dilatation of the cervix. In these disproportion cases I am unable to predict in advance of labor, with any dependable degree of success, which patient will deliver herself and which patient will require a cesarean. An adequate test of labor in each case is the only dependable approach to the problem.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—Dr. John Polak once replied to a question I asked as to what constituted a test of labor, "If you have a woman having regularly recurrent uterine contractions, with full dilatation of the cervix, or a cervix which is dilatable, with no advancement of the head after two hours, something is wrong regardless of what the measurements are." We do cesarean sections if the patient has a cervix that is dilated or dilatable and relaxed, if there is no advancement of the head after two hours of regular uterine contractions.

I have been investigating the statistics of home obstetrics in that territory comprising the area of the Southern Medical Association, for 1935. Do you realize that 65.63 per cent of the deliveries by physicians in this territory for that year were done in the homes? We must endeavor to get information about this subject to the men who are doing home obstetrics.

DR. M. PIERCE RUCKER, RICHMOND, VA.—It is wonderful what will happen to a cicatrized cervix when the patient is ready to go into labor. I remember a patient who as a result of treatment of a cancer of the cervix with a paste had no cervix. The whole upper part of the vagina was such a mass of scar tissue that I was unable to see any evidence of an opening into the uterus. Yet when she went into labor she had a perfectly easy, normal delivery without complications.

Quite recently I saw a patient, thirty-nine years old, who, after having borne three children, had undergone a cervical amputation. Her doctor was very much concerned about her and called me in consultation twelve hours after the onset of her labor. He reported that he had made a vaginal examination and had found only a little cicatrized dimple in the upper part of the vagina. Morphine and scopolamine were given and the baby was born in bed, even before the interne could be called.

DR. E. D. PLASS, IOWA CITY, IOWA.—So far this morning no one has offered a definition of labor. Labor to me may be defined as a succession of uterine contractions leading to the gradual dilatation of the birth canal and to the expulsion of the fetus. That definition does not include the word pain, for, as you well know, pain is not an essential part of the parturitional process. If we adopt some such definition of labor, we must modify our concept of a test of labor, and define trial labor in terms of progress rather than in terms of so many hours of pain.

DR. THOMAS B. SELLERS, NEW ORLEANS, LA.—The concept of a preliminary stage of labor is applicable to a rather small percentage of cases. Nevertheless, if accepted, it will be of value in obviating meddlesome interference. It is now very

researches of many observers have made it obvious that unskillful and ill-advised obstetric procedures result in many instances of fetal birth injuries, the commonest form of which is intracranial hemorrhage. This aspect of the question, however, has received such widespread recognition that an equally important side of the problem is often forgotten, with the result that any fetal birth injury has come to mean poor obstetrics in the minds of many of the medical profession, and, to an even greater extent, in the minds of the laity. I wish to discuss the question, therefore, from the standpoint of the problems that so frequently confront the conscientious and skillful obstetrician, who often finds himself on the horns of a dilemma and is not to be censured for many of the resulting tragedies to the fetus. Good obstetric practice frequently means that the child is subjected to danger of injury and this fact should be recognized. Moreover, the term "birth injury" should be used with caution. It may be an accurate term from the medical standpoint but is liable to convey a wrong impression to the laity, to whom the term is often synonymous with poor obstetrics. A patient was recently delivered on our service by outlet forceps, after an episiotomy. Labor had lasted twelve hours in the first stage and two hours in the second stage. The baby was a microcephalic child and died within two weeks. It was transferred to a children's hospital where the interne asked if forceps had been used. He subsequently told the father that the baby's head was abnormally small and it would likely die. Within an hour the father was remonstrating with me because the forceps had been used and had so compressed his child's head that it would not survive.

Some brain injuries, like the above case, are not the result of birth trauma at all, but are developmental defects or brain aplasias. Such cases may easily be mistaken for traumatic injuries without careful investigation. The use of such terms as "forceps delivery," "difficult labor," "breech presentation," etc., has too frequently placed the obstetrician in the difficult position of disproving his responsibility for many fetal cerebral conditions. Since the advent of encephalograms, many cases of cerebral atrophy, some with a history of normal delivery and others with a history of difficult labor, have been discovered. It is likely that developmental disturbances of the brain are more frequently the cause of symptoms than has usually been considered.

Even intracranial hemorrhage may be present and not be the result of trauma. One patient in our series was delivered at term, but before labor commenced, by cesarean section, the indication being a previous section. The baby died of intracranial hemorrhage, and at autopsy there was also diffuse hemorrhage in the peritoneal cavity. We know of two other cases of babies born by section who died with clinical evidence of intracranial hemorrhage. It has been shown that hemorrhagic disease of the newborn is a factor in some of these cases. Margaret Warwick'

THE RELATIONSHIP OF FETAL BIRTH INJURIES TO OBSTETRIC DIFFICULTIES*

WILLIAM A. SCOTT, M.D., TORONTO, ONT.

IN THE two years 1935 to 1936 on the Obstetrical Service of the Toronto General Hospital there were 1,710 births, and of these 77 were stillbirths and 41 neonatal deaths, a combined rate of 6.9 per cent. Any patient who is six months or more advanced in pregnancy is admitted to the obstetric wards, and our figures include some babies weighing less than 2 pounds.

An analysis of stillbirths and neonatal deaths, totaling 118 cases, included 15 macerated fetuses (several premature); 14 deformities, incompatible with life; 34 prematures, under four pounds; 1 case of pemphigus; 1 case of ieterus gravis; 5 placenta previa; 3 accidental hemorrhage; and 1 craniotomy on a dead baby.

For these 74 fetal deaths, the method of delivery could not be held responsible, with the possible exception of the 5 cases of placenta previa.

Of the remaining 44 cases for which the method of delivery may be held responsible, there were 19 normal deliveries, including 1 bronchopneumonia of mother, 1 heart disease of mother, 4 eclamptic toxemias, and 4 prematures over 4 pounds and under 6 pounds. Also 13 forceps deliveries (3 intracranial hemorrhages), in 3 eclamptic toxemias, 1 brow, 1 face, 3 persistent occipitoposterior, and 5 for delay in second stage. Among 6 versions, there were 4 intracranial hemorrhages; in 3 breech deliveries, 1 intracranial hemorrhage, and 3 cesarean sections were done, 2 before labor commenced, and 1 after three hours labor.

Of the 19 normal deliveries, 10 were complicated as enumerated. Of the remaining 9, 2 had intracranial hemorrhage (autopsy, labors 37 and 24 hours); 3 causes unknown (no autopsy), and 4 causes unknown (autopsy).

Of the 11 cases of intracranial hemorrhage (6 autopsy and 5 clinical diagnosis), there were 4 versions (2 for transverse presentation), 3 forceps (1 high, 1 mid, 1 low), 1 breech, 1 cesarean section, and 2 normal deliveries.

A review of the clinical histories of these fetal deaths appeared to emphasize some facts worthy of consideration.

The problem of fetal birth injuries is intimately connected with that of maternal mortality, and it is unfortunate that the methods to lower the incidence of one may not have the same effect on the other. The

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This was a patient, thirty years of age, who had had two previous pregnancies, the first a miscarriage and the second a low forceps delivery. There was some question whether that child had an intracranial injury but at the present time it is quite healthy at the age of five years. The patient attended our antenatal clinic, and at seven months a breech presentation was corrected by external version. She was admitted to the hospital in February with false labor pains which disappeared. Two weeks later she entered hospital in labor, having had irregular pains for twenty-six hours. The first stage lasted a further twenty hours, during which time the contractions were irregular in time and intensity. At the end of the first stage the fetal head was in midpelvis and the body lying L.O.A. She was allowed to go four hours in the second stage during which time contractions were moderately strong but occurring at irregular intervals of from five to eight minutes. Little progress was made but the fetal heart remained regular at 120-140. At the end of this period midforceps were applied and a relatively easy extraction performed. The child breathed spontaneously, was a good color, and for twenty-four hours appeared to be quite normal. On the second day a left facial palsy was noted and from then the symptoms progressed and the baby died on the sixth day. Autopsy revealed a bilateral laceration of the tentorium cerebelli with large subdural hemorrhages in the posterior fossae and also well-marked subarachnoid hemorrhages in both parietal regions.

It would appear to us that the prolonged labor in this case was responsible for at least part of the fetal injury, for it is unlikely that the diffuse subarachnoid hemorrhages in the parietal regions were the result of the forceps delivery. Yet this prolonged labor was not due to disproportion but rather to irregular and ineffectual uterine contractions. On the other hand, it is almost certain that the tears in the tentorium and the subdural hemorrhage were the result of the operative delivery. The question in our mind is whether an earlier forceps delivery might have avoided the damage.

In our series there were 21 cases in which labor lasted from twenty-five hours to four days, but in a careful review of the histories one cannot feel that attempts to shorten the labor would have been wise, except the possible use of forceps slightly earlier in the second stage in three instances (4, 4, 4½ hours). In these 21 cases there were other causes of fetal death in many instances, but the prolonged labor was probably a factor in most of them and certainly the cause in some.

If, then, prolonged labor is dangerous to the baby and attempts to shorten labor equally so, we find ourselves confronted by the question of cesarean section in the interest of the child. It is our opinion that too many sections are done with the idea of lessening the risk to the child, forgetting that with the lower fetal mortality from cesarean section, there is a corresponding increase in maternal mortality. The idea of a section to lessen the risk to the child is not new in either medical or lay literature. Laurence Stern published his *Tristram Shandy* in 1759, and in that amusing novel we find the argument for cesarean section in the interest of the child. His idea that the eldest son is usually the greatest blockhead in the family is hardly substantiated by history. Among

found bleeding in other organs in 53 cases of intracranial hemorrhage. Today the obstetrician is in an unenviable position when he encounters such a case. If the delivery were instrumental that is blamed; if forceps were not used it is often suggested that the patient was allowed to go too long in a labor that should have been terminated.

We recognize that intracranial hemorrhage is usually traumatic in origin, but it may occur in so-called normal labor. In our series 2 followed spontaneous deliveries. Moreover, many babies suffer injuries not severe enough to cause death, but some of these give evidence of their injury in later life. The human fetus is not as mature at term as the fetus is in the lower animals. Injuries from the stress of parturitional forces may be bruises and abrasions, damage of the viscera, nerve injuries, depressions and fractures of the skull bones, and intracranial edema and hemorrhage. The latter, particularly, may occur with normal labor and spontaneous delivery. During labor a large proportion of children suffer some injury, for even the caput succedaneum is evidence of superficial injury, whereas a cephalohematoma is indicative of more extensive damage. As pregnancy nears term the fetal blood becomes more venous and during labor there is a retardation of the uterine circulation with each pain, and a corresponding diminution of the oxygen supply. Pressure on the fetal head forces out some of the blood with a relative cerebral anemia and asphyxia. Occasionally this is increased by the pressure of the head on a low lying placenta. In ordinary labors the process of molding takes place without severe injury resulting, but if the force is applied too suddenly or is carried beyond a given point, tearing of the internal ligaments occurs. Even without gross damage to the tentorium or falx cerebelli there may be hemorrhage inside the skull. It is common to find small hemorrhages along the sutures, under the periosteum and in the dura. Many of these are the result of asphyxia and not of a torn vessel, although a congested vessel is more liable to rupture than one not congested. It has been stated that some traumatic effect of labor on the brain can be demonstrated in 90 per cent of all newborn infants coming to autopsy. Rydberg,² however, has pointed out that in the central nervous system of the newborn child, the presence of fatty substances can be demonstrated in varying quantities. They are extracellular and have accumulated around the glial cells, the latter being unaltered. These substances are not pathologic. In cases of acute brain injury there are fatty changes within the glial cells, and it is difficult, by any method of staining, to differentiate such fat from the extracellular fat in a given section.

We have briefly reviewed some of the factors concerned in fetal injury during normal labor. Let us now consider abnormal labors.

Prolonged labor increases the incidence of intracranial hemorrhage but so do attempts to shorten these labors and here, especially, we see the doctor's dilemma. May I illustrate with the history of another case?

little can be done except to see that the patient does not become dehydrated nor her strength exhausted. Certainly no attempt at delivery from below should be made until the cervix is completely dilated. Labor should be terminated by forceps delivery if the second stage is prolonged, but again we will encounter a certain unavoidable fetal mortality, although the latter will be lower with skilled than with unskilled attention. Forceps, or version with extraction, before the cervix is dilated only adds to the risk of both mother and baby. Three of the deaths in this series were in cases of persistent occipitoposterior position with forceps delivery.

The incidence of intracranial hemorrhage in breech cases is particularly high and is frequently the result of poor obstetrics. The idea, so widely held until comparatively recently, that haste was essential as soon as the child's hips were born, led to many unnecessary birth injuries. The aftercoming head has had no opportunity for molding to take place and forceful efforts at rapid extraction are very liable to result in intracranial damage. Nevertheless, with the greatest skill in the world, breech presentations will still carry with them a higher mortality than vertex presentations. The proper use of forceps on the aftercoming head is often a means of avoiding fetal injury. Three of our deaths were in breech cases, one of them having intracranial hemorrhage.

Transverse presentation usually has only one method of treatment, namely, podalic version. Many of these babies are dead when the patient is first seen and the mortality is necessarily high in the others. Three cases in this series were transverse presentations and were delivered by version. A clinical diagnosis of intracranial hemorrhage was made in two, but autopsies were not obtained. The third case had an autopsy and death was due to asphyxia and not to hemorrhage.

The antepartum hemorrhages are so dangerous to the mother that the child's welfare is of secondary importance. In severe cases of accidental hemorrhage the child is practically always dead, and in those of lesser severity the infant mortality is very great. In placenta previa, unless routine section is done, about 25 per cent of the children will not survive and even if section is done the mortality is still high. Three of our deaths occurred in cases of accidental hemorrhage. One was delivered by low forceps and autopsy revealed no cause of death. The others were normal deliveries and autopsies were not done. There were five deaths in cases of placenta previa, three patients were delivered by section. One had a normal delivery and autopsy showed only atelectasis. The other patients were delivered by version (transverse presentation) and a clinical diagnosis of intracranial hemorrhage was made.

From a consideration of this series of fetal and neonatal deaths, it would appear that the following views are justifiable.

1. A statistical consideration of birth injuries following any type of delivery is of little value unless accompanied by a study of all the clin-

others, Newton, Lincoln, Leonardo da Vinci, Harvey and Goethe were all first born sons. We believe there is the occasional case where section, is justifiable, in the interest of the baby alone but we think such cases are not common. Moreover, babies born by elective cesarean section do not always live and some have serious intracranial hemorrhage. I have already noted one of the latter from our series, and of the total deaths three were delivered by section.

Closely allied to the problem of long labor is the elderly primipara with rigid soft parts and inefficient uterine muscular power. These cases probably present more difficulty in private practice than they do on a public ward service. They approach labor with trepidation, to which is added an insistence that it shall be neither prolonged nor painful. This insistence is often the result of uncritical articles in the lay press describing some method of "painless childbirth." In addition, therefore, to the ordinary causes of asphyxia, there is often the effect of drugs for the relief of pain and ill-advised attempts to deliver too soon. Much can be done to prepare the minds of such patients for labor, and the absence of relatives from her room during labor makes good obstetrics easier. The fact remains that many of these women do have long labors and some of them have injured babies. We do not think, however, that cesarean section is often indicated, in the absence of disproportion. We believe, rather, in conservative obstetrics with careful attempts to relieve pain but without a routine attempt to produce "painless labor."

The commonest obstetric difficulties leading to fetal injury are disproportion, malpresentations, antepartum hemorrhages, and eclamptic toxemia. With careful antenatal supervision, only the minor degrees of disproportion will play much part in fetal injuries, for the cases of major disproportion will be detected before labor and appropriate measures adopted. When considering the induction of premature labor in such cases, it is to be remembered that the premature child is more liable to intracranial damage than is the child at term.

The minor degrees of disproportion present a very real danger to the fetus unless one is willing to see a great increase in cesarean section in such cases. It has been amply demonstrated that the great majority of such patients will deliver themselves spontaneously or can be delivered by easy forceps operations, but their labors tend to be long and the child's head is subjected to more than ordinary molding. Moreover, the size of the child is not always the same in successive pregnancies, and this may be the determining factor in the presence or absence of intracranial injury. We believe that proper obstetrics requires conservative methods with these patients, but we hold that opinion in the full knowledge that there will be a certain number of injured babies.

Malpresentations also increase the danger to the baby. Persistent occipitoposterior positions are the commonest form. Labor is prolonged and frequently ends in operative delivery. If the first stage is prolonged,

2. Immediate repair of old injuries: (a) cervix and perineum in a series of 150 cases; and (b) cystoccele, rectoccele, cervix, and perineum in 20 cases.

These two groups are compared with a series of 150 cases with evidence of old injuries, but in which no repair was done.

In these cases, I have included none with known evidence of toxemia or infection prior to delivery, but have included normal deliveries as well as forceps and versions. All are hospital cases, where ample facilities and assistance are at hand to inspect each vaginal tract and carry out such operative procedures as are deemed advisable.

IMMEDIATE REPAIR OF NEW INJURIES

The first group of cases includes a group of 300 primiparae in 70 per cent of whom there was definite evidence of trauma varying from laceration of the cervix, vaginal wall, and vulva to perineal separation and episiotomy. The greatest number of cervical and vaginal wall lacerations occurred in posterior positions of the fetal head whether labor was terminated normally or by operative interference; next in order were breech deliveries, followed by versions and anterior positions.

Regardless of our individual belief as to the subsequent occurrence of malignancy in these lacerations, we do know that their neglect results in ectropion, ulceration, infection, chronic discharge, and irritation. For these reasons I believe the present-day attitude¹ of repairing all such injuries before the patient leaves the hospital is to be commended. However, the question arises as to when this repair should be done and how extensive an operative procedure should be carried out in the puerperal state.

In our experience, we have found in this series of cases that immediate examination² of the vaginal tract and repair of *new*³ injuries to the cervix, vaginal wall, and the perineum yields satisfactory results in most cases. Cases in which examination was omitted fall mostly in three groups, viz., those in which the patient's general condition was unsatisfactory or dubious; those in which we had reason to doubt rigid asepsis; and those cases which manifested free bleeding from an atonic uterus.

INTERMEDIATE REPAIR

The intermediate operation^{4, 5} after an interval of five to ten days was used in a limited number of cases, but we found that the psychologic effect on the patient was unfavorable; the exposure was less adequate; tissues, though less edematous, were still highly vascular and more friable; and we were disturbing a healing process that nature had already instituted.⁶ The patient was subjected to a second anesthetic and her hospitalization prolonged eight to fifteen days so that economic advantages are lost.

ical facts in each case. For instance, the statement that a certain percentage of a series of fetal deaths followed forceps delivery is of little value unless we know whether there was any alternative method to forceps delivery and when and how the forceps were applied.

2. Some intracranial hemorrhage occurs frequently in so-called normal labors, and in many cases causes no symptoms.

3. Some patients having clinical evidence of such injury recover and present no evidence of permanent damage.

4. The incidence of severe injury increases with the length of labor and also with attempts to shorten labor by operative delivery from below.

5. The danger to the mother from cesarean section must not be forgotten when thinking of the danger to the child from vaginal delivery.

6. The increasing number of elderly primiparae and the desire for short and painless labors are factors in infant mortality at the present time.

7. Many serious injuries to the child are the result of either unwise or unskillful operative deliveries.

8. In many cases there is inevitable danger of serious injury to the child in a properly conducted labor; the conscientious obstetrician can only do that which he thinks is in the best interests of both mother and child.

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GYNOPLASTIC REPAIR FOLLOWING DELIVERY*

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IT IS assumed that the duty of the obstetrician at the time of delivery is not only to prevent any unnecessary injury to the mother, but also to repair any injuries that cannot be prevented. Based upon this assumption, many opinions have been expressed as to the time and the extent of such gynoplastic repair. Personal observations lead me to believe that there must be an evaluation of the pathology, both as to type and extent; a knowledge of the nature and type of operative procedure required for a satisfactory result; and an accurate appreciation of the patient's condition, so that maternal mortality and morbidity will not be increased nor convalescence unduly delayed.

The discussion touches upon the following subjects:

1. Immediate and intermediate (5 to 10 day delay) repair of new injuries in a series of 300 cases.

*Read at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20 to 22, 1937.

with a thin fascial structure as compared with the thick fascia of the abdominal wall or elsewhere in the body. Furthermore as a result of delivery this tissue is distorted, shredded out, and friable, so that even though we know what we are looking for, in its distorted form, recognition is not always easy but even at times impossible. Due to vascularity exposure is less adequate, friability makes the tissues more difficult to handle after they are identified and such structures are hastily united without the careful precision that should be found in plastic operations.⁹ It is readily conceivable that tissues distorted by pregnancy and traumatized by labor and delivery could be perforated in repair or show faulty anatomic union after involution has taken place.

In this small group of cases, we had 5 patients with cystitis and pyelitis and 4 with cystitis alone. Upon subsequent examination, there was still evidence of cystocele and urethrocele in 7 cases and in five cases there was definite evidence of rectocele. Hospitalization was increased to an average of twenty-one days; morbidity was increased and the blood pictures likewise showed an unfavorable comparison.

TABLE I. BLOOD PICTURE

	BEFORE DELIVERY			AFTER DELIVERY		
	R.B.C.	W.B.C.	HG	R.B.C.	W.B.C.	HG
N. R.*	4,091,000	12,300	82%	4,259,000	8,400	85.0%
P. R.	3,960,000	11,900	81%	3,850,000	8,900	77.5%
C. R.	4,000,000	12,800	83%	3,300,000	11,400	73.0%

*N. R., No repair (150 cases); P. R., repair of cervix and perineum only (150 cases); C. R., cystocele, rectocele, cervix and perineum (20 cases).

Founded upon theoretical objections and substantiated by unfavorable immediate and late results in those few cases of extensive repair that I have been able to observe, my opinion coincides with those who favor the interval operation performed after the patient has recovered from her delivery and after involution is complete.

However in selected cases, where there was no contraindication in the patient's condition before delivery or especially *after* delivery, our results in repair of perineum alone, or cervix and perineum¹⁰ show satisfactory anatomic results in 75 per cent of cases. That the end results are not universally good is evidenced by irregular hypertrophy and fistulous tracts seen in some cases. Experience and improvements in technique may, in time, further decrease the number of such unfavorable results.

PROCIDENTIA

Despite the fact that the cervix and perineum are properly repaired and the uterus pushed upward, by pressure above the symphysis, we often find on subsequent examination that these patients have varying degrees of procidentia. This I believe is due not so much to relaxation or subinvolution of the uterine ligaments, but rather to a destruction or

Therefore for these reasons we have discontinued the delayed or intermediate type of operation, except in a few cases where there was a contraindication to an immediate operation or where there has been a breaking down of a perineal repair.

REPAIR OF OLD LACERATIONS AFTER DELIVERY

The second group of cases, viz., the repair of old lacerations and injuries resulting from previous deliveries, is more controversial and admits a greater diversity of opinion. For that reason it is well to enumerate (1) the various conditions found during pregnancy as well as immediately after delivery; (2) the various operative procedures carried out; and (3) a résumé of our end results both immediate and late.

The conditions found most frequently are lacerations of the perineum, cervix, cystocele, urethrocele, rectocele, and varying degrees of procidentia. It is admitted that delivery is one operation and repair of these conditions is another, but one which requires time, care, and precision as well as the ability of the patient to withstand prolonged anesthesia, additional blood loss, possible shock and lowered resistance. The question arises, can operative procedures for the correction of all these conditions be carried out routinely, or, can only a limited type of repair, e.g., trachelorrhaphy and perineorrhaphy,⁸ be carried out in selected cases?

Satisfactory end results are judged by the criterion of end results obtained from operations on the nonpuerperal patient. Economic advantages to the patient or the community do not justify mortality, morbidity or inferior end results.

As there was no mortality in this group of 150 cases of cervical and perineal repair after delivery, a comparison will be made with an equal group of 150 cases in which, for various reasons, no repair was made. These cases will be compared from the standpoint of morbidity, blood picture on admission and discharge, days of hospitalization and presence of nonfebrile complications, e.g., subinvolution, anemia, bladder and rectal complications.

At this time suffice it to say that there was a slight increase in morbidity, an average increase of two and one-half days of hospitalization, a definite though not serious change in the blood picture and an increase in the number of bladder complications.

REPAIR OF CYSTOCELE AND RECTOCELE

Before taking up the third group of 20 cases in which a more extensive type of repair was carried out, it is well to recall that cystocele is a hernia of the bladder through the anterior vaginal wall due to a separation of the supporting fascia. Likewise, rectocele is a hernia of the rectum through the separated posterior vaginal fascia and proper repair requires that this fascia be identified and united before closing the vaginal mucous membrane. In this case as in cystocele, we are dealing

catgut No. 2 are placed about 1 cm. apart starting from the upper angle and continuing to the external os. The opposite side is treated in the same manner. We have found better results since using a running suture in the mucous membrane, the first loop of which is placed deeply above the apex of the laceration, and then continued down the line of incision and over the end of the cervix for a distance of 1 cm. where it is tied. The pack is then removed from the uterus and the vagina swabbed with tinct merthiolate. The posterior vaginal wall is grasped at the mucocutaneous border with Allis' forceps and the scar tissue is excised. The vaginal mucous membrane is then dissected upward and levators exposed. All scar tissue is excised, and levators and fascia united by interrupted chromic catgut sutures. Excess mucous membrane is excised and the cut surfaces approximated as in the usual perineorrhaphy. Skin is closed by a subcuticular catgut or by interrupted dermal sutures.

If the cervix lies low in the vagina or protrudes at the vulva, the uterus is pushed upward and a gauze pack inserted loosely in the vagina. This pack, introduced with a tubular packer, is removed at the end of thirty-six or forty-eight hours.

If the patient is unable to empty her bladder she is catheterized every eight hours and irrigated with silver nitrate 1 to 10,000 once daily.

In exposing the cervix we avoid pushing the uterus down from above, as we believe this adds additional trauma to the loose areolar fascia supporting the cervix and upper vagina. Likewise, care must be used not to tear the cervix or pull it forcibly through the vulva so as to facilitate its suture.

COMMENTS

Delivery is one operation and gynoplastic repair another. The latter is a hospital procedure with many limitations to be carried out on selected cases with the aid of capable assistants observing rigid aseptic technique.

Recognition of gross cervical and perineal injuries is usually not difficult; exposure can be obtained with comparative ease without additional trauma; excision of previous scar or traumatized tissue is quickly carried out and fresh surfaces united by suture in a short time. The procedure cannot be carried out routinely, but is subject to many limitations, the most important of which are the general condition of the patient following delivery and the extent of the pathology. The primary object of the obstetrician is a successful delivery and no procedure which increases maternal morbidity and mortality can be condoned in this age of critical scrutiny.

That there are economic advantages in examination and immediate repair of certain injuries, one cannot deny, likewise many subsequent pathologic changes can be prevented. The anatomic results are not universally good and subsequent examinations at times show marked irregular hypertrophy of the structures repaired.

CONCLUSIONS

1. The vaginal tract should be examined after every delivery if there is no contraindication from the standpoint of asepsis or the general condition of the patient. New lacerations and injuries should be cared for at that time.

faulty anatomic union of the fascia supporting the lower parts of the uterus and upper vagina. That such fascia does offer the greatest support to the uterus seems established from experiments of the past few years. With this thought in mind various methods were used to temporarily hold the cervix in a relatively normal position until natural healing or coaptation was established. While no method is free from practical and theoretical objections, nevertheless, a rather simple one has caused the patient less discomfort, has been productive of no increased morbidity and has yielded fairly good results.

ELEVATING CERVIX AND SUPPORTING UTERUS

In cases where the cervix presents at the vulva or lies in the lower vagina, it is grasped with a ring forceps and the uterus is pushed upward with the hand above the symphysis. A large tubular packer is then used to insert 3 to 5 yards of gauze around the cervix and gently fill the vagina without protruding through the vulva. This packing is inserted firmly but not tightly as one would to control hemorrhage. The sponge forceps is then withdrawn and the pack allowed to stay in place for thirty-six to forty-eight hours.

This is not done in any case where the integrity of asepsis is doubted or where any previous infection was known to have existed. Likewise, it is not offered as a curative method for cystocele, rectocele, or procidentia, but just as predelivery emptying the bladder and rectum helps to avoid injury to these structures and their fascial supports, so also this procedure seems to have some merit in causing the fascia of the lower uterus and upper vagina to reunite in a more normal position.

TECHNIQUE

Preparation for repair of new and old birth injuries is really begun as early in the prenatal period as is found any evidence of infection or injury from previous deliveries. Cervical and vaginal infections are cleared up by appropriate treatment, and in the case of old injuries, the patient is told that if circumstances are favorable, after delivery, correction of certain conditions will be attempted. However, she is told of the possibility of the procedure not showing a perfect result, but we feel that, if the operative procedure is limited to cervical and perineal repair, a satisfactory result may be obtained in 75 per cent of the cases.

Immediately after delivery all instruments and utensils used in the delivery are discarded; new gowns and gloves are to be used and the patient redraped with sterile linen, after spraying with tinct merthiolate. The vagina is retracted either with a self-retaining weighted speculum or exposed with retractors in the hands of assistants. The cervix is grasped with four ring forceps and the entire circumference inspected. A gauze pack, with string attached, is inserted into the uterus to keep back any uterine bleeding. Any new laceration of 1 cm. or over is sutured and even smaller lateral lacerations are caught with one interrupted suture. In the case of old lacerations, the side with the deeper one is treated first and all previous scar tissue is excised both from the anterior and the posterior lip. As the anterior lip is usually thicker than the posterior the edges are trimmed so the surfaces to be approximated are nearly the same size. Then interrupted sutures of the chromic

woman who has given birth to a baby has done her good deed for the day, and no avoidable burden should be placed upon her. With this thought in mind, I would say to Dr. King, and to all who follow his precepts with equally good results, "You have proved your ability to get reasonably good results and are justified in continuing on." But to those less skilled, who are not so situated as adequately to safeguard their patient, I would say, "Be content with the repair of the fresh wounds in the pelvic floor and await the time of complete involution before proceeding with the repair of injuries to the cervix, of cystoceles, urethroceles, rectoceles, and procidentia." All this in the interest of better obstetrics.

DR. J. BAY JACOBS, WASHINGTON, D. C.—Figures bearing much resemblance to Dr. Scott's are those published this year by Küstner of the Leipzig Clinic. In the delivery of 7,319 children occurring in the last two years, 81.4 per cent were normally born and of these 3.8 per cent were stillborn or died during the first week. Of the children delivered by operative procedure, 16.2 per cent died.

As concerns the frequency of intracranial injury, Bland reported 27 per cent in which bleeding was present. Holland found laceration of the tentorium cerebelli in 48 per cent of cases examined. Occasionally bleeding does not accompany laceration. Prematures, whether delivered normally or operatively, are especially subject to intracranial damage due to weak blood vessel walls and incomplete development of meningeal fibers.

The production of intracranial injury is said to be due principally to factors that cause alteration in the shape of the skull.

In this respect it is instructive to cut a window in both parietal bones of a still-born fetus thus permitting the removal of the brain and enabling observation of changes occurring in the falx cerebri and tentorium cerebelli, when pressure is applied in the various diameters of the fetal skull. It is noted that these membranes are less liable to stretch and tear when transverse compression is applied, as in the cephalic application of forceps, than when pressure is applied obliquely. And when compressed in the anteroposterior diameter, little effort is required to stretch and rupture these membranes. Where vessels are not severed, the prognosis is more favorable.

A most noteworthy observation is brought to our attention by L. H. Smith of Portland who performed cisternal punctures in a large series of normal infants at birth as well as many who encountered some intracranial damage. Blood was found in the spinal fluid in both types, but its presence was of no prognostic importance, as was determined after a five- to seven-year follow-up of the mental and physical facilities of these children. He concluded that only the degree and character of the clinical signs and symptoms are important in arriving at a diagnosis and prognosis of birth injury.

In 1936 I reviewed several hundred case records, classifying them into normal, precipitate, and prolonged labors, and operative deliveries. Each of the patients had been delivered ten years before, of parents of approximately the same social status, age, environment, and intellectual capacity. Various intelligence tests were made on all these children, and it was found that all, regardless of the type of labor or delivery, rated about the same. Also the incidence of illness was similar for the two groups. Thus, there seemed to be no intellectual or physical retardation. It appears safe to assume, then, that only the major degrees of intracranial injury are liable to produce a mental or physical defect that remains permanent.

DR. RUDOLPH W. HOLMES, CHICAGO, ILL.—As regards primary repair, I believe there should be a survey of the whole parturient canal after each operative

2. In selected cases and under favorable conditions immediately after delivery, repair of old cervical and perineal injuries can be carried out with little difficulty. The immediate and late results are usually satisfactory.

3. The immediate operation offers advantages from an economic and psychologic viewpoint, while the intermediate operation has the additional disadvantage of disturbing tissues that have already started to heal.

4. Extensive repair of cystocele, rectocele, and enterocele as well as cervix and perineum is an operative procedure requiring more time and precision than is advisable after delivery. Such operations should be delayed until the patient has fully recovered from her delivery and the tissues have undergone complete involution.

5. Repair of cervix and perineum do not prevent procidentia and uterine displacements. This can be done only by restoration of the fascial attachments in their normal relationship. Surgical restoration at this time is inadvisable and a simpler method should be sought. Loosely packing and distending the vagina with gauze following delivery seems to accomplish this in some cases.

6. Both the immediate and intermediate operations present technical difficulties not present in the interval operation, but if performed in selected cases and limited to the cervix and perineum can be commended as having definite advantages to the patient.

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DISCUSSION ON PAPERS OF DRS. KING AND SCOTT

DR. PALMER FINDLEY, OMAHA, NEB.—Let me say at the onset of my discussion that I have no quarrel with any man who obtains reasonably good results in adopting any operative procedure. Dr. King has demonstrated in his statistics that he can do just that. But what of the general practitioners who are doing the bulk of obstetrics? Can we expect of them equally good results? I think not. And if it be true that the extended repairs advocated by the essayist would be hazardous in the hands of the inexperienced operator, should this Association go on record as endorsing such a procedure in routine practice? It is scarcely conceivable that morbidity and mortality will not be increased if the methods proposed by Dr. King are accepted and practiced by the general profession, yes, and by the experienced obstetric surgeon.

In the first half of my professional career I endeavored to learn what to do, and now in the second half I am learning what not to do. To my way of thinking, a

We all encounter cases of ovarian hypo- or hyperfunction associated with the presence of ovarian tumors, especially retention cysts. Some of these are thin walled, may be easily ruptured by bimanual pressure, or the function may be restored by aspiration of the contents of the cyst through the cul-de-sac.

My interest in the surgical treatment of ovarian dysfunctions, other than those associated with ovarian tumors, was aroused by a clinical and pathologic study published by the late M. R. Robinson of New York, in 1935. At this time he presented 7 cases, 4 of ovarian hyperfunction and 3 of hypofunction, in all of which he obtained gratifying results by resecting the major portion of both ovaries, in a wedge-shaped manner.

Robinson's explanation of the beneficial effects obtained is as follows:

"In ovarian hyperfunctions the morphologic changes in the sex gland and in the endometrium represent the effects of the pituitary hyperstimulation with follicle-ripening hormone. The character and degree of the morphologic responses varies with the phase of the dysfunction. A surgical removal of a sufficient amount of ovarian parenchyma harboring an excess of morphologic and biologic elements responsible for the existing functional disturbance, permits the pituitary to regain its intraglandular balance and thus a restoration of a normal pituitary-ovarian correlation."

He also maintains that in ovarian hypofunctions the reverse holds good. "Here the luteinizing forces of the anterior hypophysis play the leading rôle. The inhibitory effect of the ovary in this type of dysfunction is upon the already weakened follicle-ripening properties of the hypophysis. A removal of sufficient amount of ovarian parenchyma containing these disturbing elements helps in the restoration of a normal intrahypophyseal balance, and thus a return to a normal pituitary-ovarian correlation." He maintains there is a pattern to the pathological changes which is uniform in character.

A review of the literature reveals very little material on this subject, except that presented by Robinson.

After reading this report it occurred to me that I had seen a number of cases of ovarian hypofunction, in which the ovaries were frequently small and very tender, which I thought might have been benefited by excision of the thickened ovarian cortex without destroying the parenchyma. Those patients had not had the advantage of modern endocrine therapy. That phase of our treatment is even now of inconstant value, i.e., the methods of treatment are not entirely standardized. Furthermore the results obtained by endocrine therapy are not always what one might hope for.

The excision of a large segment of ovary in the treatment of hyperfunction may be considered justifiable. However, with one exception I have limited my surgical treatment of these patients to those showing evidence of hypofunction at the time of operation. However, two of these had presented the picture of ovarian hyperfunction on previous occasions.

intervention to ascertain what damage may have been done. Necessary repairs should be made. In the absence of hemorrhage, I have rarely sutured the cervical tears, other than very extensive ones. As regards secondary repair immediately following delivery, I took the stand thirty-five years ago that extremely rare circumstances should dictate such a procedure.

The parturient canal is teeming with bacteria. All the parturient tissues are in a state of physiologic congestion, comparable to the first stage of an inflammatory process. The canal is covered with innumerable minute abrasions, and veins and lymphatics are patent. Heedless manipulations may be the means of disseminating the bacteria with disaster.

Immediately post partum the parturient canal is a widely patulous cavernous tract. When involution has been completed, the canal becomes a perfectly physiologic and anatomic vagina. I question the ability of any one so to gauge a secondary repair immediately post partum that the woman will have a normal canal after involution is complete. I have had some instances of this post partum secondary repair of so-called cystocele and rectocele where the canal became so contracted that marital relations were impossible.

DR. KING (closing).—This is certainly not a procedure to be advocated routinely, or used in unfavorable circumstances, but under favorable conditions in hospital practice our results do justify the type of repair I have advocated. This I know is likewise the experience of many members of this Society, who have not only carried out but have advocated gynoplastic repair of old lacerations of the cervix and perineum for many years.

DR. SCOTT (closing).—It is quite obvious that if there is an indication for operative delivery there will be some difficulty and there will be more danger of damage to the child. If we are to do conservative obstetrics, we must accept some inevitable fetal mortality, for if we attempt to prevent that mortality by radical methods, for instance, cesarean section, then we shall have some maternal morbidity.

SURGICAL TREATMENT OF OVARIAN DYSFUNCTIONS*

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THE past few years have seen phenomenal changes in our conception of the functions of the various endocrine glands. Theoretically the ovarian dysfunctions have all been explained and appropriate medical treatment should correct the difficulty.

Unfortunately there are many patients who do not respond in any way to endocrine therapy, and it is a small series of these cases of which I am about to speak, and hope to stimulate some discussion on your part as to whether or not the surgical measures employed are to be considered justifiable.

*Read at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20 to 22, 1937.

abdomen which had been decidedly worse in the previous two days. The menstrual history was that she had menstruated slightly every two or three months since childhood, with some pain.

Examination showed the presence of a cyst of the right ovary; the uterus was small and firm. She was admitted to Lakeside Hospital April 10, 1936, with the diagnosis of ovarian cyst with dysfunction. At operation a chocolate cyst of the right ovary approximately 5 cm. in diameter was found; right salpingo-oophorectomy and incidental appendectomy were performed. Inspection of the left ovary showed it to be small, with a very thick cortex; almost the entire cortex was excised and the ovary suspended. There were small cysts present in the ovary without evidence of recent ovulation. She last reported on Aug. 30, 1937, that her menstrual periods were now every twenty-four days, lasting three or four days, and without pain.

CASE 3.—Mrs. L. S., aged thirty-two years, para ii. This patient was first seen in consultation, March 12, 1932, complaining of irregular bleeding since the birth of her second baby, Nov. 5, 1931. Examination showed some relaxation of the vaginal outlet, the uterus was in slight retroversion, both ovaries moderate in size and very tender. The uterus was brought into place and a Smith pessary inserted. Two days later she menstruated, with a severe hemorrhage, and four days after this was admitted to Lakeside Hospital, complaining of severe pain in both ovaries; the ring had been removed. She was treated with bed rest, douches, and tampons; examination showed the right ovary to be irregularly enlarged and exquisitely tender. March 21, 1932, the polycystic part of the right ovary was resected. July 19, 1932, four months later, this patient was again seen with her family physician, now having very severe pain in her left ovary, requiring opiates for relief. A long series of antuitrin-S and other gland therapy followed this procedure. Pain in the left ovary persisted without reference to ovulation, and the patient became a semi-invalid.

Examination April 24, 1935, almost three years later, showed the left ovary to be small, polycystic, and extremely tender. She was readmitted to the hospital at that time, and the left ovary was exposed through a left gridiron incision. The ovary was found to be polycystic but small, the cortex was resected and the patient made an uneventful recovery. On Aug. 28, 1937, this patient reported that she menstruated regularly, in moderate amount, and had no more ovarian pain.

CASE 4.—Mrs. F. H., aged thirty-eight years, nullipara, married twelve years. This patient was seen Sept. 6, 1936, complaining of amenorrhea, sterility, and general malaise. Her last menstrual period had been in 1926. Examination showed a small atrophic uterus; ovaries likewise very small. She was given an intensive course of theelin therapy, also thyroid by mouth. She was admitted to the University Hospitals, Nov. 3, 1936, and was operated upon the following day. A dilatation and curettage were performed, with the insertion of a small stem pessary. Upon opening the abdomen, both ovaries were found to be atrophic, with greatly thickened cortices, almost cartilaginous in structure. The cortices were excised. She made a normal recovery. She was placed on emmenin and theelin therapy but had not menstruated to date. However, she says that she feels better than she has for many years. She is still receiving endocrine therapy.

CASE 5.—Mrs. R. K., aged thirty years, nullipara, married seven years. This patient was first seen Oct. 4, 1933, complaining of sterility. She gave a history of menstruating every ten to twelve months. She had been given fourteen injections of theelin and antuitrin-S without results. Physical examination showed a small, healthy woman; however, she had a male type pelvis and male hirsutes. Pelvic examination showed the left ovary slightly large and tender. Basal metabolic rate was -1 per cent. She was placed on small doses of thyroid and pituitary extracts and ten days later had a slight menstruation. She had a slight flow in November,

The operation consists of the following:

The ovary is grasped at either pole by Allis forceps, and the cortex incised longitudinally from one end to the other, for a depth estimated to be sufficient to extend through the width of the thickened cortex. The cortex is then taken off the parenchyma by sharp dissection, denuding a half or two-thirds of its surface. Bleeding is somewhat annoying, and is controlled by means of mattress sutures of 00 plain catgut, not unlike the method of obtaining hemostasis in a subtotal thyroidectomy. No attempt is made to bring the cut edges of the cortex into approximation.

If the ovary is somewhat prolapsed, as it often is, it is suspended by means of a reef stitch of chromic gut, taken in the ovarian ligament, or the organ is loosely attached to the fundus. Care is taken that no interference is caused in the ovarian blood supply.

CASE REPORTS

CASE 1.—Mrs. C. L. (University Hospitals), aged twenty-one years, para i. This patient first came under my observation July 19, 1927, complaining of one-child sterility. General examination showed a short obese woman, weighing 180 pounds. She had had one child born three years before this date. She further complained of a gain of weight of 40 pounds in three months' time and that menstruation occurred every seven or eight weeks, free and without pain, but she had some dull pain in the left side of her lower abdomen.

Examination showed the uterus to be large and boggy and the left ovary large, polycystic, and tender. In September, 1927, dilatation and curettage were performed at Lakeside Hospital; at this time a Rubin test was positive. After this she continued to have pain in the cystic left ovary and was given twelve very light doses of x-ray to the ovary which was then advocated, but without relief. Severe nosebleeds followed this. In 1928 she reported that her menstrual periods were more regular, but the pain was persistent and had become bilateral. In August, 1929, she reported no menstrual period for the previous six months. Basal metabolic rate was -4 per cent at this time, she was given intensive gland therapy and placed on a diet for obesity.

She was next seen in December, 1934, then twenty-eight years of age, weighing 170 pounds, complaining of spotting or actual bleeding constantly, for six months. On Jan. 5, 1935, a dilatation and curettage were performed at Lakeside Hospital. The pathologic diagnosis was hyperplasia of the endometrium. She had continued to have pain in both ovaries, but upon examination they were not large. A month later she reported no vaginal bleeding but had had a nosebleed twice a day. Regular menstrual periods followed until July, 1935, when they ceased.

In February, 1936, her basal metabolic rate was -20 per cent and she was given intensive endocrine therapy, but her pains continued. On May 6, 1936, operation at Lakeside Hospital consisted of a diagnostic dilatation and curettage, excision of the cortices of both ovaries, and incidental appendectomy. At the time of operation the ovaries were 5 by 4 by 3 cm., studded with many tiny cysts thought to be immature Graafian follicle cysts; two-thirds of the cortex of each ovary was removed. On April 10, 1937, the patient reported she was feeling better than she had for many years, had lost 19 pounds in weight without intensive dieting, and menstruated in moderate amounts six days of each month and had no more ovarian pain. On Sept. 7, 1937, she reported she was feeling fine; menstrual periods as above noted.

CASE 2.—Mrs. A. C., age twenty-three years, nullipara, married three years. This patient was first seen April 9, 1936, giving a history of severe pain in the lower

PATHOLOGY

Robinson maintained that there are definite morphologic changes linked with the functional changes in all cases of long standing.

A careful pathologic study of the material removed in our five cases of decortization for hypofunction was made by Dr. Robert Faulkner. He summarizes his findings as follows:

On pathologic examination of the ovarian tissue removed, three characteristics were common to all except one. First, thickening of the tunica albuginea; second, increased fibrosis of the ovarian cortex; third, follicles in all stages of development and atresia.

Where curettings were available, normal physiologic phases prevailed with no particular phase predominating. One endometrium was of the "Swiss cheese" hyperplasia gland pattern. In the ovarian findings of follicles and fibrosis, there was one exception, a persistent corpus luteum with cystic dilatation.

Therefore, these cases show no absolutely constant histologic features in the ovaries. Such characteristics as are present are in general almost opposite those catalogued in cases of ovarian hypofunction by Robinson. Inability to definitely classify ovarian findings in the dysfunctions seems logical for the reason that seldom is any dysfunction purely ovarian in character, but only a part of the general endocrine derangement.

SUMMARY

I have presented five cases of ovarian hypofunction, with ovarian pain, all of whom were benefited by excision of one or both ovarian cortices. Another case, of hyperfunction with pain has apparently been relieved functionally and subjectively by excision of part of each ovary, combined with almost complete decortization.

Surgical treatment of ovarian dysfunction should have a very limited field of usefulness, but it is my opinion that there is a place for it if we are to utilize all the facilities at our command. Many of these patients become actually psychic, due to almost constant pain, and with their inordinate fear of the consequences of abnormal sex functions.

Partial decortization alone appears to be beneficial in relieving ovarian hypofunction, and pain.

Excision of a segment of ovarian parenchyma, usually without decortization, may be beneficial in some obstinate cases, in dealing with hyperfunction.

A combination of the procedures might be undertaken if ovarian pain accompanies hyperfunction.

1933, none in December and developed headaches. In February, 1934, a stem pessary was inserted in the uterus. Sixteen days later the patient had a normal menstruation and her headache stopped. The pessary was removed February 26 because of excessive bleeding. On June 30, 1934, the patient reported there had been no menstruation since the stem had been removed, so we replaced it. Her next menstrual period was November 17, five months later, and on Dec. 3, 1934, the stem was again removed. On March 30, 1935, the patient reported no menstruation since November, 1934, and complained of severe pain in the left ovary, present for two weeks. Examination at this time showed the left ovary enlarged and very tender. She was admitted to Lakeside Hospital, March 31, 1935, and on the following day April 1, dilatation and curettage and stripping of the capsule of the ovaries and incidental appendectomy were performed. She made an uneventful recovery from the operative procedure and menstruated twenty days after the operation, freely and without pain, for three days (April 20). She again menstruated May 30 and July 12 and reported she felt better than for many years. She menstruated August 30, September 30, and November 5 and continued at thirty- to thirty-five-day intervals until April 30, 1936. July 22, 1936, examination showed her to be two months pregnant. She was delivered March 1, 1937, by low cervical cesarean section, of a living male baby, at full term. Section was done because of the male type pelvis in which the head had not engaged. At this operation both ovaries were inspected and a small omental adhesion separated from the left one. A very thin bluish cortex had re-formed on both ovaries. At this time she had been married eleven years.

On Aug. 23, 1937, this patient reported that she now menstruated every thirty-five days, freely, and has no more ovarian pain.

CASE 6.—Mrs. A. S., aged twenty-three years, para i. This is a case of hyperfunction at the time of operation, in which a modification of the aforementioned operation was employed.

She was referred to our service for therapeutic abortion from the Tuberculosis Sanatorium of the Cleveland City Hospital, on May 5, 1936. She was then two months pregnant, and therapeutic pneumothorax treatment had been instituted. The abortion was performed, and she was later discharged to the Out-patient Department.

She at no time had had any evidence of tuberculous disease other than pulmonary. She gave a menstrual history of frequently missing menstrual periods since their onset, at the age of fifteen years. She was readmitted to the sanatorium Sept. 10, 1936, and had begun to menstruate. This became very free, in spite of intensive treatment with antuitrin-S and ergotrate, and on September 30 a dilatation and curettage were performed. Hyperplasia of the endometrium was found.

She was seen in the Out-patient Department on April 4, 1937, with the history of prolonged and irregular menstruations following the dilatation and curettage. She had then been bleeding constantly since Feb. 28, 1937. Examination showed the uterus very small, and anterior, both ovaries large and very tender, especially the left.

She was readmitted to the Hospital April 27, 1937, still bleeding, and on May 3 was operated upon. This consisted of a dilatation and curettage, resection of a segment of each ovary, and decortization of approximately two-thirds of the remaining portions. She made an uneventful recovery. Therapeutic pneumothorax therapy had been continued throughout this time.

She reported July 20, 1937, that her menstrual periods were now regular every thirty days, lasting seven days. Examination now shows both ovaries small and no longer tender.

The pathologic report of this case noted the presence of large numbers of tiny follicle cysts in the excised ovarian tissue.

croached upon the blood supply of the ovary, causing an enlargement of the organ. If this occurs within a reasonable period of time, the reason for the increase in size is presumably known. This is the only instance in which bimanual rupture might be excusable, even though it is not without attendant danger. I have seen in fact a case in which this procedure was accomplished so successfully that the patient had to be subjected to abdominal section in order to stop the hemorrhage from a corpus luteum cyst. Aspiration through the culdesac is likewise a dangerous procedure on account of the possibility of disseminating malignant cells. We all know that the grade of malignancy in an ovarian cyst does not depend upon its size or age.

Dr. Reycraft stated that after denuding one-half to two-thirds of the ovarian cortex, no attempt was made to approximate the cut edges. In this respect may I mention the value of a free omental graft. It prevents the adhesion of intestine to the line of excision, as well as the adherence of the ovary to the parietal peritoneum or a pelvic viscus. It in no demonstrable manner interferes with ovarian function.

PROFESSOR DANIEL DOUGAL, MANCHESTER, ENGLAND.—I am particularly interested in Dr. Reycraft's paper because two years ago one of my colleagues, Dr. K. Vernon Bailey, reported a series of cases of secondary amenorrhea treated by splitting or "extroversion" of the ovaries. His paper was received with a good deal of skepticism and I personally thought that in some of the cases menstruation would have returned spontaneously without any surgical treatment.

More recently, Bailey read a further communication and claimed that he was able to cure 70 per cent of, I think, 20 cases. One of the patients with a history of two years amenorrhea menstruated regularly for a few months after the operation and then became pregnant. These were astonishing results and the discussion on Bailey's paper was on similar lines to the one we have had today. Bailey's method was to split the ovaries and stitch them in such a way that the two halves were left opened out, with the raw surfaces directed downward toward the floor of the culdesac where presumably they became adherent. This appeared to be a somewhat crude procedure but was evidently quite successful.

The ovaries treated were either cystic or had a thickened cortex. I confess that I am rather skeptical when I read about the ovarian cortex being thickened and I would like to know what standards the pathologists apply when determining this fact. It is claimed that these operations facilitate ovulation but I think that the results must be due to stimulation of functional activity by traumatizing the ovary.

Dr. Reycraft's methods and results come as a shock to those of us who believed that with increased knowledge of physiology the treatment of ovarian dysfunction was becoming more logical, and must be taken as an indication that the pendulum is swinging back again. This may not be a bad thing if it helps us to realize that ovarian function can be restored by other methods than endocrine therapy.

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DISCUSSION

DR. WILLIAM H. WEIR, CLEVELAND, OHIO.—Dr. Reycraft's concluding remarks, that there is a limited field in surgery for these dysfunction cases, sum up the situation. The fact that Dr. Reycraft has obtained satisfactory results shows that his cases were adequately studied, suitable patients selected for operation, and endocrine treatment thoroughly tested beforehand.

My own results when I undertook abdominal operations for such conditions were usually bad. The temporary results might be good but they were not lasting. We formerly were accustomed to puncture follicle cysts, to split the ovarian capsule, or to resect a piece of ovary. These operations would permanently benefit an occasional case but the average case was improved only temporarily. A great many of them were made definitely worse because we had then not only a polycystic ovary for example, but an adherent one as well.

I cannot quite reconcile in Robinson's article, which Dr. Reycraft quotes, the removal of ovarian tissue for conditions due both to supposed hypofunction and also hyperfunction. I gathered from the paper that the purpose of the operation was simply to remove a certain amount of ovarian tissue so that the balance between the pituitary and ovarian reactions would be more normal. If that is the case, it would seem simpler to remove part of, or the whole of, one ovary, and allow the other ovary to remain untouched, thus lessening the danger of postoperative adhesions. On the other hand, is the operation done with the intention of removing the unduly thickened cortex in the hope that the new scar tissue that replaces it will be less dense and so permit the rupture of follicles, developing in the underlying area?

In these patients we should be very conservative, especially if retention cysts of the ovary be present. Many individuals come to me, after they have had immediate abdominal operation advised. In the interval of a day or more between the examinations of the original physician and of myself, a large follicle cyst, for example, may have spontaneously disappeared. These cysts of the ovary should be treated conservatively and watched for a while, for the follicle type of cyst will seldom need operation.

DR. FRED M. DOUGLASS, TOLEDO, OHIO.—One point I would like to bring up is the morbidity that follows leaving a raw surface. Regardless of the care taken in raising the ovary out of the pelvis, difficulty will follow any such procedure. I believe this morbidity must be weighed in analyzing or summarizing the end results.

The few treated in this way shows that Dr. Reycraft is not attempting operation upon every patient with ovarian pain. I am sure that he does not want to leave that impression. I would like to have Dr. Reycraft speak a little further on the late results if he has observed any of these patients over a long period of time.

DR. T. K. REEVES, PITTSBURGH, PA.—Dr. Reycraft has stated that some of these cysts are thin walled, may be easily ruptured by bimanual pressure, or the function may be restored by aspiration of the contents of the cyst through the cul-de-sac. Is it justifiable to rupture a pelvic mass without knowing the exact nature of the mass? Probably many here, in removing the uterine tubes, have inadvertently en-

and a vaginal douche of 1:3000 solution of permanganate of potash should be given twice a day until the infection is reduced. The use of mandelic acid internally may be of great assistance, as many of these organisms are very rapidly overcome by this drug (Braasch²).

Just before cystoscopy is begun the bladder is irrigated with boric acid solution and a bivalve speculum is introduced and the vagina dried out, taking care not to cause bleeding from the sensitive bladder mucosa that protrudes through the fistula. Then the introitus is closed with the subcuticular suture. A bladder that has been decompressed over a long period of time will be hard to distend, but as the bladder and vagina are distended together, the fistulous opening can be viewed and if the ureteral orifices can be seen, No. 6 ureteral catheters should be passed if possible. A phenolsulphonephthalein function test is then done to note the comparative kidney function. If the ureteral openings cannot be visualized, an intravenous dose of indigocarmine is given and its excretion watched for from both ureteral orifices. If this is found to be unsatisfactory, an intravenous urography should be done. If only one kidney is functioning, and that on the same side as the fistula, the probabilities are that the ureteral opening is in close proximity to the fistula and the greatest care must be taken not to constrict the ureter at operation.

If it is possible to insert catheters in the ureters, they should be left in situ and an operation performed within twenty-four hours.

METHODS OF REPAIR

I have had no experience with transvesical or transperitoneal repair. Both of these methods may have their place in certain types of cases and have resulted in success after several vaginal route failures. The one advantage pointed out by Sears³ in the transvesical operation is the possibility of ureteral catheterization at the time of operation, and the care that can be taken by this method to prevent ureteral obstruction. However, Everke⁴ operating by this method failed to put catheters in the ureters and tied both of them. Uremia developed and the patient died.

TREATMENT OF VESICOVAGINAL FISTULAE*

CAMERON DUNCAN, M.D., BROOKLYN, N. Y.

VESICOVAGINAL fistula is of infrequent occurrence at the present time. Phaneuf¹ estimates that it occurs once in ten thousand gynecologic and obstetric cases. The small number of cases treated by any one clinician makes it hard to arrive at definite conclusions and a perfect operative technique, and the operative treatment is so frequently unsuccessful that a consideration of the handling of this distressing condition may not be out of place.

ANATOMIC CONSIDERATION

The anterior vaginal wall is about 7.5 cm. in length. The posterior vaginal wall is about 10 cm. long. The female urethra is 3.75 cm. in length. The ureteral openings are 3 cm. from the bladder neck or internal urethral opening.

The length of the urethra, plus the length of the bladder neck to the intraureteric ridge or top of the trigone is 6.75 cm. which leaves about 1 cm. of bladder wall in approximation to the anterior vaginal wall above the trigone.

After panhysterectomy, at least from 0.5 to 1 cm. of vaginal wall has been amputated. That would bring the remaining vaginal vault on the level of the trigone and ureteral openings.

As a postoperative fistula nearly always occurs at the point where the vagina is amputated, that fistula is then in close proximity to the ureteral openings. And, if it is not in the median line, it is in close proximity to the ureteral opening on the side nearest the fistula. Occlusion of the ureter by suture or undue kinking may happen very easily (Case 1).

There is one other anatomic factor worth considering. The vaginal wall is a modified skin, of tough structure, with very little muscle tissue. It is about 0.5 cm. thick. The bladder wall is a muscular organ and in its collapsed state is 1 to 1.5 cm. thick. There is very little fibrous tissue in the bladder wall and so it is not prone to form much cicatricial tissue. The vaginal skin is very fibrous and forms the same type of scar tissue as the skin on the outside of the body.

CYSTOSCOPIC EXAMINATION

When the fistula is small and the bladder can be distended with fluid, cystoscopy can be done without any difficulty. But when the fistula is large and the fluid introduced into the bladder runs out of the fistulous opening as fast as it is introduced, cystoscopy is impossible. To overcome this, the vaginal introitus can be infiltrated with 1 per cent procaine solution and a subcuticular suture of heavy silk or linen is taken around the entire vaginal outlet and tied very tightly to make the vagina watertight. Proper preparation of the bladder and the vagina should precede this method of cystoscopy. If infection exists, the bladder should be irrigated daily with a saturated solution of boric acid

*Read at the Fiftieth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20 to 22, 1937.

DRAINAGE

For the ordinary fistula well above the bladder neck, the indwelling Pezzar catheter kept in from seven to ten days is sufficient. Where the fistula is low down near the bladder neck, a plain catheter sutured in as suggested by Phaneuf is the desired method. When the patient has had repeated operations which have resulted in failure, a suprapubic cystotomy, with a large Pezzar catheter No. 30 or larger sutured in, is a satisfactory method of drainage.

As the intravesical pressure is the same in all directions and there is no pool of urine but a closed sac full of fluid, the position of the patient in bed is of no consequence. The essential thing is to see that there is no kinking of the drainage tube or catheter and that there is no pull on the catheter to cause discomfort to the patient or to pull the catheter out of the bladder.

The following case illustrates the importance of preoperative urologic study with cystoscopy and intravenous urography.

CASE 1.—M. M., forty-three years old, colored; admitted to hospital Jan. 17, 1936. She had had a panhysterectomy and bilateral salpingo-oophorectomy for fibroids and chronic pelvic inflammation six months before, by one of my assistants. She had a vesicovaginal fistula 0.5 cm. in diameter to the right of the median line in the vaginal vault. There was no preoperative urologic study done. The laboratory findings were normal except for a slight increase in the total blood urea of 39 mg. in 100 c.c. of blood. She was operated upon Jan. 22, 1936, under local infiltration of 1 per cent solution of procaine. The usual technique was carried out. She drained only 10 ounces of urine the first twenty-four hours. The next day she was acutely ill with a temperature of 105.5° F. and complained of pain in the right side of her abdomen and right loin. The resident was instructed to have a cystoscopy done and if the ureters could not be catheterized, to remove all sutures and allow the fistula to open. An emergency blood chemistry was ordered. Being encouraged by a slight increase in drainage, the cystoscopy was not done and the wound not opened. The blood chemistry showed urea 70, creatinine, 2.05, sugar 84. She was getting a saline elysis of 1500 c.c. and an intravenous infusion of 300 c.c. of 25 per cent dextrose solution daily. The elimination continued poor and on the fifth postoperative day she showed marked nitrogen retention, urea 181, sugar 228, and creatinine 2.85. A cystoscopy showed an irritable bladder, the ureteral opening could not be visualized and indigo-carmin was not excreted in fifteen minutes. A flat x-ray of the abdomen showed both kidneys normal in size and position with no opacities. Uremia was evidently developing and the sutures were removed and the fistula allowed to open on the sixth postoperative day. An intravenous urography showed no excretion of the dye in either kidney. The patient died the next day of

Allis' clamps and excised with a scalpel. This as a rule gives a better denudation than trying to excise with scissors. The elasticity of the bladder wall can then be tested by picking it up separately with Allis' clamps and drawing it together. Most of the scar tissue will be found in the vaginal skin. The vaginal wall is then separated from the bladder wall, mostly by blunt dissection. If the vaginal wall is very adherent to the bladder wall, Ward's method of incising the vaginal wall some distance from the fistula and dissecting toward the fistula is preferable. Most of the time, if the patient has not had a previous operation, the vaginal skin is easily mobilized from the bladder wall and may be incised either longitudinally or transversely as it may seem best. The vaginal wall is dissected off the bladder wall for a sufficient distance to allow closing the bladder wall with three layers of sutures. The suture material that we use is No. 00 extra hard forty-day chromic catgut, generally on a small full curved atraumatic needle. The first layer is taken through the bladder wall submucosal and is of the cross-stitch type. Any inversion of the mucosa into the wound will defeat the result. Two more layers build up the bladder wall to produce more tissue to heal together. This inverts the fistula into the bladder. If a leak should occur later, this gives a better chance for the fistula to heal spontaneously. The vaginal wall is then closed with a layer of buried sutures, catching the bladder wall to leave no dead space. The last layer closes the vaginal skin together with No. 0 chromic catgut. I can see no advantage in using silver wire to close the vaginal skin. If the bladder wound heals, the vaginal skin will heal regardless of the type of suture used. Halban⁵ is also of this opinion. We have had no experience with alloy stainless steel wire permanent sutures, and in these days of clean catgut it would seem unessential to bury foreign bodies where they might ulcerate into the vagina or bladder.

TOTAL COLPECTOMY

For the treatment of a large fistula at the vaginal vault in an old woman, either after hysterectomy or irradiation, total colpectomy and closure of the fistula is a good method.

The technique is best carried out under local infiltration of procaine. The fistulous tract is picked up and excised. The vaginal wall is then dissected away and the fistulous opening in the bladder is closed. The entire vaginal skin is then removed and the cavity is closed by numerous purse-string sutures down to the introitus. This procedure can only be done where the cervical canal is completely closed from irradiation or after a panhysterectomy (Case 2).

A subtotal colpectomy, Le Fort operation, could be done where the uterus is still in and in the place of leaving two lateral gutters for drainage, one would be sufficient.

MECHANICAL ABRASION

When the fistula is so small that it causes a leaking but the patient voids by urethra a fair quantity, a cystoscopy is done and a ureteral catheter passed through the fistulous tract into the vagina for several inches, then the catheter is caught in the vagina and quickly drawn through. A catheter that is slightly rough from age or repeated sterilizations is preferable. A fresh abrasion heals more readily than a chemical or thermic burn. There is no reason for cauterization, electrocoagulation or caustic chemicals being used in this type of case, only a fresh abrasion is justified (Case 3).

catheter was passed through the fistula into the vagina. Not wanting to withdraw the catheter through the bladder for fear of infection it was picked up in the vagina and quickly drawn through. A few days later, the fistula healed.

CONCLUSIONS

1. The bladder wall is far more elastic than the vaginal wall, and contains so much muscular and elastic tissue that the scar tissue in vesicovaginal fistulae is mostly confined to the vaginal wall.

2. After hysterectomy or irradiation most fistulae are in close proximity to the ureteral openings.

3. Cystoscopy should precede operation, the ureters should be catheterized and kidney function tests be done, including intravenous urography.

4. A method of cystoscopy in fistula cases has been described.

5. Free mobilization of the bladder from the vagina is essential.

6. After thorough repair of the bladder wall, the method of closing the vaginal skin is unimportant.

7. Complete or partial colpectomy is applicable to large fistulae.

8. Mechanical abrasions should be tried in small fistulae before resorting to operation.

9. Suprapubic bladder drainage is advisable in patients who have had repeated operations or where the fistula is near the bladder neck.

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DISCUSSION

DR. LOUIS E. PHANEUF, BOSTON, MASS.—Where the bladder cannot retain fluid for a cystoscopic examination the Kelly endoscope used in the knee-chest position may render great service. Without too great difficulty, the ureteral orifices may be located, the ureters may be catheterized and the visualization of the relationship of the fistulous area may be accomplished. This instrument, which was in common use up until twenty-five years ago, should not, in my opinion, be entirely abandoned.

The importance of the renal function test is obvious when we realize that most of the surgical fistulae follow difficult panhysterectomies, and because of the inaccessibility of the deep structures about the cervix, the ureter of one side or the other is not infrequently inadvertently tied. The proximity of the vesicovaginal opening to the ureter in surgical fistulae has been brought out in the paper.

In the nulliparous woman with a small introitus and narrow vaginal tube, I have found that bilateral episiotomies gave better exposure than a single incision, no matter how extensive, on only one side. The free mobilization of the bladder, as pointed out, may be obtained by large vaginal incisions longitudinal and transverse. Occasionally, a combination of the two may simplify the approach.

I am a strong partisan of the metallic suture, having used silver wire up to 1935 when I learned from Dr. W. Wayne Babcock of the greater advantages of the alloy

The following case illustrates total colpectomy in a large fistula in an old woman after radium irradiation.

CASE 2.—L. M., sixty-four years old, colored widow, had had irradiation of Roentgen rays and radium for carcinoma of the cervix a year previously. She was admitted with the carcinoma completely healed, the cervical canal completely imperforated, and a large vesicovaginal fistula 1.5 cm. in diameter at the vaginal vault. A cystoscopy was attempted but was unsatisfactory as the filling solution ran out as fast as introduced. Suturing the vaginal outlet did not occur to us then. She was operated upon under local procaine infiltration. An extensive mediolateral episiotomy gave ample exposure. The usual technique was carried out and after the bladder was repaired the entire vaginal wall was removed and the cavity closed with numerous purse-string sutures. A Pezzar catheter was inserted in the bladder and left in for twelve days. She made an uneventful recovery.

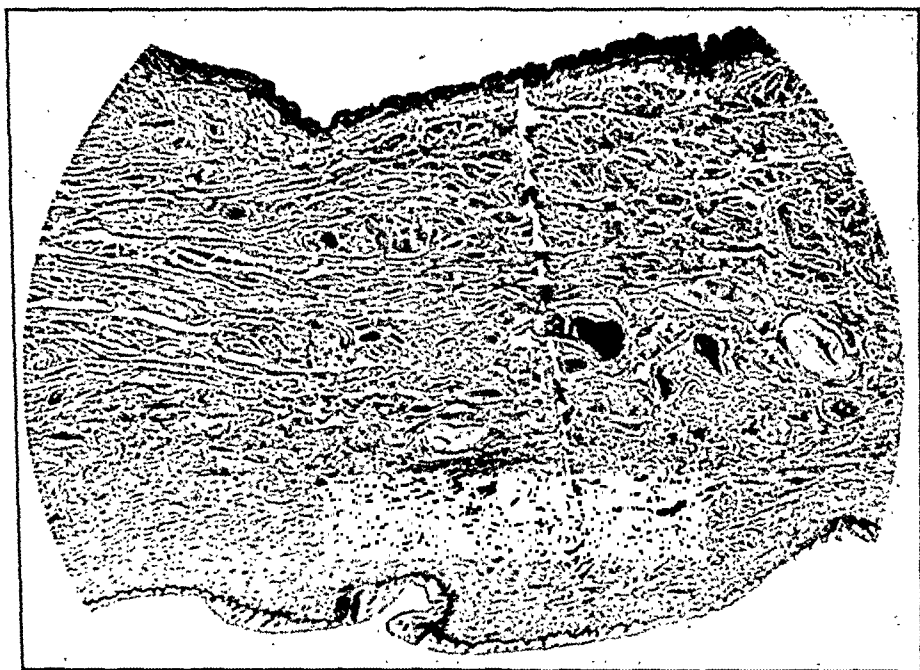


Fig. 1.—A section taken through the bladder wall and the anterior vaginal wall above the trigone, $\times 12$. Above is the bladder mucosa with several layers of transitional epithelium. The longitudinal, circular, and oblique muscle bundles of the bladder wall are lying in a soft fibroelastic bed. Below is the modified skin of the vaginal wall with its dense structure and covered with its thick squamous epithelium. Between the bladder wall and the vaginal wall are many large blood vessels and nerves.

The following case illustrated the value of mechanical abrasion of a small vesicovaginal fistula.

CASE 3.—C. C., forty-seven years old, white woman, had had a vaginal hysterectomy for adenocarcinoma of the corpus uteri two months previously. She was admitted with a small vesicovaginal fistula 0.5 cm. in diameter at the vaginal vault. It was repaired with the usual technique, and she was discharged from the hospital on the tenth postoperative day with the fistula healed. About a month later she began to have a slight leaking of urine from the vagina. She was advised to return for a second repair but refused. After two years I succeeded in getting her to come to my office for a cystoscopy. The bladder wall was normal; on the intraureteric ridge a small fistula was seen having almost the appearance of a third ureteral opening. A

PELVIC TUBERCULOSIS*

JAMES E. KING, M.D., BUFFALO, N. Y.

DURING the past ten years, definite progress has been made in our knowledge of tuberculosis. A number of factors has contributed to the present decrease in infection and increase in cures. These are: a better understanding of juvenile tuberculosis and its significance in adult pulmonary and extrapulmonary infection; the earlier diagnosis of pulmonary infection; the value of sanitarium treatment; surgical procedures and principles in the treatment of pulmonary cases, and the education of the public in the importance of hygiene and in the dangers of contact with pulmonary tuberculosis.

Tuberculosis may affect any organ or tissue of the body and, like syphilis, it thus possesses an interest for every practitioner and every specialist. Inasmuch as pelvic tuberculosis is known to constitute from 5 to 8 per cent of all cases of pelvic inflammation, its importance to the gynecologist is obvious. No practitioner or specialist should essay to treat any form of tuberculosis unless he is familiar with the more recent advances in our knowledge. The purpose of this paper is to investigate some of these in order to determine which may be applied to the better understanding of the etiology, diagnosis, and treatment of tuberculosis of the pelvis.

A new interest was stimulated in tuberculosis in 1882 by the discovery of the tubercle bacillus. Since that time, a voluminous literature has accumulated. The majority of contributions have appeared in French and German, relatively few in English.

The development of a comparatively safe operative technique has made it possible for the gynecologist to understand the gross pathology, and to study clinically both early and late cases of pelvic tuberculosis. There is still much uncertainty in diagnosis, and a failure on the part of some surgeons to appreciate the significance of certain phases of its etiology upon which are based the principles that should govern its treatment.

ETIOLOGY

For a number of years, a lively discussion has been going on as to whether pelvic tuberculosis is, or ever can be, a primary local infection, or whether all cases of vaginal and cervical tuberculosis, together with uterine and tubal involvement, are to be regarded as a secondary infection from a primary focus in some other part of the body. Much argument, speculative and theoretical, and many case histories, have been

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suture. Since that time, I have used the alloy suture with great satisfaction and I am firmly convinced that I have closed difficult fistulae with metallic sutures that I could not have closed with catgut. Thus far, I have not seen ulceration in the bladder and vagina as the result of their employment.

Since reporting 10 personal cases of vesicovaginal fistula at our 1935 meeting I have operated upon 3 others, making a total of 13. The first had a supracervical hysterectomy for pelvic tuberculosis; the right ureter had been tied and the bladder had been injured at operation. She had had one attempt at closure before she came to consult me. She was operated upon suprapubically, reaching the bladder extraperitoneally. The portion of the bladder removed histologically showed tuberculous cystitis. As might be expected, my repair which held for a few days was not successful. Her left kidney shows good function and I intend to close her vagina at a later date.

The second was a large obstetric fistula. The bladder was closed with the finest alloy sutures and the vagina with coarser ones, which were removed, healing taking place by first intention.

Finally, the third patient, a nulliparous woman with a small introitus and narrow vagina came to me from another state for a fistula which had immediately followed a panhysterectomy for fibroids. By means of bilateral episiotomies, free mobilization of the bladder, alloy sutures in this organ and the vagina, I was able to obtain primary healing. This patient was operated upon four weeks ago.

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—A fistula is not often due to incision in the bladder but to traumatization with subsequent sloughing. This is indicated in the lapse of time between the original operation and the appearance of leakage.

I wish also to emphasize the use of the Kelly instrument. I do not think any gynecologist is satisfactorily equipped to view the inside of a bladder without it. With this we do not have to rely upon fluid to distend the bladder. Catheterization of ureters should be universally done in patients with large fistulae.

I have not used malleable wire in bladder fistulae, but I have had a very beautiful result in an old complete perineal tear by using the alloy suture, the case having once failed in its repair.

DR. DUNCAN (closing).—The Kelly endoscope can, I agree, be used for ureteral catheterization in a bladder that will distend with air under ordinary atmospheric pressure with the woman in the knee-chest position. In these fistula cases, however, the bladder has been decompressed for so long that it has become contracted and, even with the vagina closed with suture, it is hard to distend the bladder under water pressure to hold more than two ounces. It may be possible that the ureteral openings cannot be visualized and one must resort to an indigocarmine test to watch for its excretion. All this takes time and it is very uncomfortable for a patient to remain so long in the knee-chest position. I think the water filled bladder and a regular cystoscope will be found more satisfactory.

are many sources of contamination by strains of acid-fast, nonpathogenic bacilli found in plants and animals (Rabinowitsch⁷) and in the air and water (Brem⁸) that cannot be differentiated by smear from the tubercle bacillus.

Corper and Vidal⁹ approached the problem from the experimental side. They injected virulent strains of human, bovine, and avian bacilli into the blood of guinea pigs, rabbits, dogs, and chickens. They found that the injection of high concentrations of 1.00 mg. into the blood stream of a susceptible animal invariably produced death within a month, and at all times the bacilli could be recovered from the blood. When, however, the same bacilli in the same dosage were injected into animals that were not susceptible, the bacilli disappeared from the blood stream within a few days following the injection. It was also found that upon injections of the more attenuated doses, 0.001 to 0.000,001 mg., the bacilli disappeared promptly from the blood stream even of susceptible animals, although these doses might produce a generalized tuberculosis. These investigators conclude that there is no evidence for the belief that tubercle bacilli multiply in the blood. They also believe that when the tubercle bacillus finds entrance into the blood stream of man, it will, as a rule, disappear quickly, and that the various forms of surgical tuberculosis are to be regarded as embolic implantations of the bacilli. It would appear that these views coincide with what is known clinically of genital tuberculosis.

This conception of blood borne infection in surgical tuberculosis at once arouses interest in the possible location of a primary focus. It is generally conceded that such a focus is most frequently in the lung. The relative infrequency, however, of bone, kidney, cerebral, and genital involvement in sanitarium patients manifesting all degrees of pulmonary involvement, would cause one to wonder why surgical tuberculosis does not occur with greater frequency in these patients.

Greenberg,¹⁰ in his review of 200 cases of pelvic tuberculosis, quoted autopsy findings upon tuberculous women by various European observers who found from 1 to 8 per cent with pelvic involvement, while Stopper found 20.5 per cent and Posner 30 per cent.

The discrepancy in these percentages raises a question as to the reliability of some of the observations. In various reports dealing with series of cases of pelvic tuberculosis, only about 25 per cent have had demonstrable evidence of pulmonary involvement. I found that in my 26 cases of the past twelve years, 6 gave evidence of pulmonary tuberculosis. It is clear that the extent of pulmonary involvement plays at most but a small part.

Inasmuch as practically all pulmonary cases show regional lymph node involvement, these glands offer a second possible source of bacteria. It would seem that, in the number of cases of pelvic tuberculosis showing no demonstrable evidence of pulmonary invasion, the primary focus in a considerable proportion originates in the bronchial lymph nodes. Whether found in lungs or lymph nodes, however, it may be assumed that either the bacilli enter the blood stream only as a result of some comparatively rare combination of circumstances, or that if the bacilli do enter the blood stream frequently, they disappear, as has been shown, before embolic implantation takes place.

brought forward in support of possible primary infection. Those who oppose this view, cite the extreme rarity of such vaginal and cervical infection, even in long-standing cases of extensive pulmonary tuberculosis, where opportunity for the introduction of infection is always present. Norris¹ feels, as do others, that the infrequency of such local infection is due to the protective character of the vaginal epithelium, but admits the possibility of infection in the case of injury to the vaginal or cervical epithelium.

Jameson,² in a monograph published in 1935, reports two series of experiments to establish the possibility of primary infection. The procedure in his first series was to insert pledgets of cotton, saturated with a virulent strain of tubercle bacilli, into the vaginas of 12 normal guinea pigs. The tampons were placed in ten of the animals during estrus, at which time the vagina is believed to be more susceptible to infection. The tampons were retained in the vagina for several days by lightly applying a Michel clip. At the end of one hundred days, the animals were autopsied and the regional lymph nodes and the genital organs were studied carefully. In only one animal did there appear any genital tuberculosis, and that was a lesion of the cervix. This one and four others, however, showed definite lymph node invasion. Feeling that somewhat different results might be obtained in sensitized animals, 15 guinea pigs were sensitized by injecting tubercle bacilli into the axillary glands. After allowing several weeks to elapse, bacilli were introduced into the vagina by the same method as in the former series. In this latter group of animals, the results were quite different. Nine of the guinea pigs showed submucous lesions of the vagina, 4 lesions of the cervix, and 1 a large abscess of the uterus. Jameson states that these results were strikingly like those obtained by Granzou in similar experiments. From these findings he concludes that an occasional primary infection of the vagina and cervix may occur, at least in sensitized individuals, but that a primary infection ascending to the uterus and tubes must be exceedingly rare. While the possibility of primary infection of the vagina and cervix may be admitted, it is generally accepted that intrapelvic infection by the tubercle bacillus is always blood borne.

Naturally, many have attempted to discover the presence of the bacillus in the blood. Weichselbaum in 1884 found the bacilli in smears of postmortem blood clots. In 1908, Stäubli³ and a number of other Germans searched for the bacillus in hemolyzed blood and in 1909 several German investigators claimed to have an almost 100 per cent success in smears from sedimented blood of tuberculous patients. These methods and results failed to find general acceptance.

Attempts to recover the germs from the blood by culture were also made, but Wilson,⁴ writing in 1933, was able to collect only 6 undoubted instances of successful blood cultures up to 1929. In 1930, Löwenstein⁵ of Vienna revived interest in blood cultures by reporting the results he obtained in many thousand specimens of blood. He claimed a surprisingly high percentage of positive cultures. These positives he described as "macroscopic" and "microscopic." His work aroused a new interest in bacillemia, and a number of investigators attempted to confirm Löwenstein's findings. The results were varied—so varied indeed, that grave doubt was expressed. So many failed to duplicate his findings that in 1930 Löwenstein⁵ felt called upon to devote an article to setting forth the reasons for these failures. Siegel and Singer,⁶ following the Löwenstein technique, were able to obtain macroscopic cultures in 1.4 per cent of 911 specimens from 422 tuberculous persons. The macroscopic cultures were proved to be virulent bacilli. Their 13 per cent of microscopic cultures obtained were not proved to be cultures of the tubercle bacilli. This is possibly accounted for by the fact that it has long been recognized that there

tuberculosis is made, it is only presumptive in the majority of instances. There are, nevertheless, a number of indications which, if sought for, may suggest very strongly the probability of tuberculosis.

The first essential necessary in making a diagnosis of pelvic tuberculosis is for the surgeon, when dealing with pelvic infection, to always keep in mind that pelvic tuberculosis can and does occur. This is self-evident, and though frequently mentioned, it may again be emphasized. In any case in which the cause of the inflammation is not determined with reasonable certainty, the surgeon should be suspicious of tuberculosis. With this suspicion in mind, he is better able to elicit facts in the history and to undertake studies that may prove to be of distinct value in suggesting the diagnosis of tubal tuberculosis.

We have often found that, had a more careful inquiry been made into the past history of the patient rather than focusing too closely upon the pelvic symptoms, much that would have been suggestive might have been learned. The history of previous pulmonary infection or a possible pleuritis is of great importance; the association with one who has tuberculosis, and finally frequent coughs and colds, may all be significant.

A careful chest examination should always be made and, in the absence of physical findings, x-ray plates, read by an expert in their interpretation, should be resorted to. Here it must be remembered, however, that a patient with chest signs may well have a gonorrheal salpingitis, and that one with evidence of gonorrheal endocervicitis may have a tuberculous salpingitis.

The positive skin tests for tuberculosis unfortunately give no clue as to the location of the lesion. With the decreasing number of reactors in the past ten years, the significance of a positive reaction has some weight in the probability of pelvic tuberculosis and a negative test definitely excludes it.

A review of recent studies of tuberculin skin tests indicates that considerable progress has been made. Many studies in the past few years have been undertaken upon children to determine the influence of their association with adults having tuberculosis. Incidentally, much has thus been learned of the relative value and the delicacy of reaction shown by the various tests.

There are three tests that have been extensively used and certain facts concerning them should be known even by those not especially interested in pulmonary tuberculosis. When Koch developed his "old tuberculin" it was used as a diagnostic agent and also as a "cure" for tuberculosis. Its use as a cure was quickly abandoned, and it was finally used only in diagnosis by means of the Pirquet scratch test. This proved to be somewhat crude. It was sufficiently definite, but was not a quantitative test. The Mantoux test is at present the one most frequently employed. It is used intradermally and its advantage lies in the possibility of accurately

The possibility that a tubal infection may result from the spread of a tuberculous peritonitis, or that a peritoneal involvement may arise from tuberculous tubes, are questions that clinicians are willing to concede.

The figures with reference to the frequency of involvement of the various pelvic organs show the tubes to be infected in about 100 per cent of the cases. Any discussion of the subject, therefore, centers about the tubes. In the majority of instances, infected ovaries have only surface implantations. The percentages of ovarian infections vary within wide limits. Such infection is practically always secondary to that of the tubes and, associated with it, involvement of the peritoneum is usually found.

In determining the frequency of uterine tuberculosis, postmortem studies of patients dying of pulmonary tuberculosis afford an opportunity for histologic study in every case. In statistics from operations on pelvic tuberculosis, the figures vary in different clinics depending upon how many patients were curetted, or upon how many uteri were removed and examined. The generally accepted figures place the frequency of uterine tuberculosis at about 50 per cent.

DIAGNOSIS

The preoperative diagnosis of tubal tuberculosis has always been recognized as being extremely difficult and, in many instances, impossible. It is unfortunate that diagnosis of early involvement of the tubes cannot be made, for I believe that early recourse to the accepted, present-day treatment of pulmonary tuberculosis would heal the early tubal lesions equally well.

The signs and symptoms of tubal tuberculosis have been frequently reviewed but no sign or symptom is found that may not be associated with other forms of pelvic inflammation. The history of the pelvic complaint will therefore help little in reaching a diagnosis. Occasionally the pain of tuberculosis may be more constant than that of gonorrheal salpingitis. This fact was brought out several times after the pathologist had made the diagnosis. The leucocyte count may be suggestive, as it is found to be lower than in similar pathology due to the gonococcus. In our experience, loss of weight is usually not present and many of the patients have shown no general effects of their pelvic pathology.

The findings on pelvic examination also give no evidence suggesting tuberculosis. Untreated tubal tuberculosis is a progressive disease and, due to this fact, various types of pelvic pathology may be found. All of these types, however, may also be met with in other pelvic infections. Frequently, even inspection of the tubes at operation will not suggest tuberculosis.

There are apparently no pathognomonic symptoms, nor any specific findings upon which to base a definite diagnosis. If a diagnosis of pelvic

in other infections. Freeing adhesions necessary for removal of the tubes is done by sharp dissection; all others are left undisturbed. Where pus is encountered, rubber tube drainage is always used. Drains were employed in 8 of my 26 cases, and no fecal fistula followed. The sinus that may follow can always be cured by appropriate measures. Finally, I am firmly convinced that every case of pelvic tuberculosis, regardless of how successful surgery may have been, should be followed by sanitarium treatment with heliotherapy. It is surprising how casually this most important part of the treatment is mentioned, if mentioned at all, by those who discuss treatment. This feature is most essential, and should always be strongly emphasized. It is unfortunate that sanitarium treatment consumes so much time, but at present there is no substitute. Following operation, the patient should be moved as promptly as possible to such an institution. The general condition of the patient will improve rapidly. A sinus, if present, will heal. What is still more important, it is the only means of healing the primary focus that has supplied the bacilli. For this latter reason, if for no other, such treatment is imperative.

It is much easier to persuade the poorer patient to undergo treatment because many of the sanatoria are maintained for those unable to pay. It is often difficult to convince a married woman that she can leave her home responsibilities. There are many arguments which, if stressed, will seldom fail to persuade a reasonable patient of the need to eliminate any remaining pelvic infection and to calcify and render innocuous the primary focus from which the infection spread. In my 26 cases here mentioned, all patients were urged to enter a sanitarium for further treatment. Fourteen acted upon this advice. One went to her home state where she spent several months in a sanitarium. Thirteen went to the city institution near Buffalo. Most of those who followed this advice were ward cases who could avail themselves of free treatment. A number of private patients and a few ward cases, for one reason or another, refused to go. A patient with a discharging sinus very seldom requires surgery. These patients with the evidence of their active infection constantly before them are easily convinced that further treatment is necessary. If the necessity of such postoperative care were more generally emphasized, less difficulty with other patients would be experienced.

SUMMARY

Progress in knowledge of tuberculosis for the past few years is reviewed in explanation of some problems of etiology.

Diagnosis is still difficult. A few suggestions are offered and the relative value of the skin tests considered.

Some views gained from experience in treatment of 26 patients in the past twelve years are presented with emphasis upon postoperative sanitarium treatment.

determining the amount of tuberculin to which the individual will react. It may be used in varying dosage. A 0.001 mg. dose will usually elicit a reaction to an active tuberculosis. Should it not, a 0.01 mg. dose may be tried, reaction to which will always indicate the presence of tuberculosis.

A still more recent test is the use of purified protein derivative, the so-called "P. P. D." test. It is supplied in one-fourth grain tablets of two strengths, 0.0002 mg. and 0.05 mg. These tablets are soluble in the salt solution supplied with them, and varying strengths can thus be prepared. Incidentally, it is of interest to note that during the two-year period from June, 1934 to June, 1936, 56,688 individuals were tested with purified protein derivative, and positive reactions were found in 47 per cent. This is a marked decrease from the 70 to 80 per cent of a few years ago. Purified protein derivative will doubtless be the choice for future tests for tuberculosis. It is intradermal and possesses all the advantages and none of the disadvantages, such as sensitization, of the other tests.

About the time Löwenstein reported his blood cultures, he proposed a skin test. It consists of the soluble substance of the tubercle bacillus, extracted with glycerine, and the whole dead bacillus. The skin is cleansed and a drop of this testing agent is rubbed in. A positive reaction consists of a nodule at the site of the inoculation. In a reactor, the nodule will appear in from twenty-four to seventy-two hours. This test is not as delicate as the Mantoux and Pirquet tests. Fine,¹¹ who did a comparative study of the three tests, concluded that, while the Löwenstein test is not as delicate as the other two tests, a reactor to it is certain to have an active tuberculosis and in his opinion it qualifies that individual for sanitarium treatment. Is it possible that such a test, being less sensitive, would be of greater value in surgical tuberculosis than the more sensitive ones?

TREATMENT

There are many excellent articles to be found on the surgical treatment of tuberculous salpingitis. It is not the purpose of this paper to discuss these, but I do wish to emphasize some points in connection with the surgery and treatment of tubal tuberculosis. I am convinced that no patient should be operated upon in the presence of fairly well-marked pulmonary involvement. This is not so much because of any objections connected with surgery itself, but because in such cases the pelvic pathology is the less serious of the patient's infections. Three or four weeks in a hospital following operation may result in extension of the pulmonary process. Radical surgery is seldom required. An ovary should be removed only when abscessed, or when it is infiltrated with tuberculosis. The surface implantations may be ignored if proper post-operative treatment is carried out. The adhesions associated with pelvic tuberculosis are so dense that, as a rule, no line of cleavage is found as

removal of tissue, because we doubted the diagnosis and this was also reported as tuberculous. In the meantime some material was injected into guinea pigs and they died of tuberculosis. The sedimentation rate was rather rapid, and it was thought best to give Elliott vaginal heat and not to subject her to surgery. At the end of three months the mass had subsided to such an extent that she was given another series of Elliott heat treatments. The mass subsided further following this and examination about a year later revealed a residual mass of thickening. She is apparently well now. I am not presenting this as a method of treatment in pelvic tuberculosis, but merely as a case which may be regarded as one of tuberculosis of the genital tract which subsided without surgical measures.

DR. F. S. WETHERELL, SYRACUSE, N. Y.—About three months ago a patient was sent to me from a tuberculosis sanitarium because of a profuse vaginal discharge. On examining her I discovered a lesion of the cervix such as I have never seen before. It was a sharply demarcated, eroded area about 1 cm. in diameter with a serpentine edge, absolutely distinct from the squamous epithelium surrounding it. The squamous epithelium looked perfectly normal, while this area was a bit darker and had the appearance of the red plush on the backs of these chairs. The report on a biopsy specimen was tuberculosis of the cervix. This is the only case of tuberculosis of the cervix that I have seen. The treatment which I suggested was the use of the quartz light. It is a rather difficult procedure to insert the light on the cervix.

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—We have at the present time at the Cook County Hospital in Chicago three patients with primary tuberculous lesions of the cervix. They have all been under observation for over two years. One patient has a complicating myoma the size of a three months' pregnancy, one has a syphilitic gumma, and the third perfectly normal pelvic organs. We have not submitted these patients to any form of treatment other than to instruct them in general hygiene and a nourishing diet.

The interesting point is that two of these patients return to us with the ulcerations completely healed, and the squamous epithelium apparently intact, but if we remove a piece of tissue for biopsy we still get a positive diagnosis from the pathologist. The other has begun to spread rapidly on to the vaginal wall and we have sent her to have x-ray therapy tried.

DR. FREDERICK H. FALLS, CHICAGO, ILL.—An interesting condition of the pelvis from the standpoint of differential diagnosis is actinomycosis of the ovary. Last year at the Cook County Hospital we had such a case which developed from a tuberculous salpingitis. The lesion appeared on one side, the opposite tube remaining completely free, a finding noted by other operators. The lesion is not like a tuberculous salpingitis but is more like a massive gonorrheal salpingitis. Of course, if the lesion breaks down, the sinus that forms shows the typical sulphur granules, but in dealing with a chronic infection of the pelvis which appears to be a diverticulitis or a unilateral salpingitis, this condition of actinomycosis must be considered.

DR. JOE VINCENT MEIGS, BOSTON, MASS.—We have had at the Pondville Hospital one patient with tuberculosis of the cervix who also had pulmonary tuberculosis.

Why is it necessary to operate on pelvic tuberculosis at all? Might these patients not get well by being sent to a sanitarium without operation?

DR. J. R. GOODALL, MONTREAL, CANADA.—I have two interesting records that I would like to detail. Years ago a child of sixteen years was brought to the hospital with a large mass in the abdomen. She had no symptoms. When the abdomen was opened, the two Fallopian tubes were enormously distended, practically

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DISCUSSION

DR. E. MACD. STANTON, SCHENECTADY, N. Y.—The very word "tuberculosis" carries with it the concept which comes to us from our experience with pulmonary tuberculosis. This concept has been confirmed by our experiences with joint tuberculosis, renal tuberculosis, and intestinal tuberculosis. When, however, we come to study tuberculosis of organs not immediately exposed to complicating secondary infections or to mechanical or chemical trauma incident to their normal activities, we are compelled to assign totally different prognostic values to infections caused by the tubercle bacillus.

To illustrate this point, let me refer to lymph gland tuberculosis. One hundred and seven personally operated cases of lymph gland tuberculosis, mostly of the cervical lymph nodes, were traced for an aggregate of 1,348 postoperative years, or an average of 12.6 years per patient. This study showed that only 4 out of the 107 had ever developed any clinically recognizable pulmonary tuberculosis. In fact, almost all of them had completely recovered. The experience of the group had thus been decidedly better as regards the development of serious forms of tuberculosis than the normal expectancy for unselected groups subjected to an equal number of years of exposure.

In a similar study of 12 cases of mesenteric gland tuberculosis discovered at operation, I was able to trace the patients for a total period of over 120 postoperative years, or an average of ten years for each case. These patients were all alive and well. Not one of them had developed any serious form of tuberculosis.

In my experience tuberculous salpingitis has been relatively much rarer than the figures quoted by most authors. In a series of 502 operations for grossly demonstrable salpingitis, I have encountered only 8 cases of tuberculous salpingitis or only 1.6 per cent.

DR. ROBERT D. MUSSEY, ROCHESTER, MINN.—Tuberculosis of the female genital organs is essentially a condition amenable to surgical treatment. However, I want to report briefly one patient who recovered without surgical measures. This young woman, a nurse, unmarried, twenty-four years of age, had a cervical polyp removed two months before coming under our care. Three or four days following removal of this polyp she had a chill, rather severe pain in the pelvis, and two or three weeks later a large amount of pus drained through the rectum spontaneously. The pain continued and when we saw her she complained of a low-grade fever, which she had recorded herself, and pelvic pain. The menstrual periods had not been disturbed. On examination the preliminary diagnosis was of a pelvic inflammatory lesion involving the left tube and ovary. Physical examination and x-ray examination of the lungs did not show any tuberculosis. Our attention was called to the possibility of some other condition by the rectal examination which revealed about 10 cm. from the anus an ulcer in the anterior wall of the rectum, which was craterlike with rather firm borders. She was subjected to a proctoscopic examination, and the tissue removed was reported as tuberculous. She was subjected to another proctoscopic re-

Editorial

Calcium Needs During Pregnancy

IN RECENT years the attention of both the obstetrician and his patient has been directed to the need of calcium, phosphorus, and vitamins during the antenatal period. No one can doubt that such attention to these dietary essentials has improved prenatal care in this country, especially as the average American diet, demonstrated by Sherman¹ many years ago, is often deficient in calcium. On the other hand, many unwarranted claims for calcium, phosphorus, and vitamin therapy have been advanced.

It is well established that the normal adult requires a minimum of 0.45 gm. and an optimum of about 0.7 gm. of calcium a day. During the last trimester of pregnancy the calcium requirements are increased to probably about 1.5 gm. per day. Absorption of calcium, in the form of soluble salts, which are formed only in an acid medium, occurs in the small intestines. In order to accomplish this, calcium may be taken in the form of milk at meals, or as calcium salts no nearer meals than four hours after and one hour before.² Furthermore, should there be no exposure to sunlight, vitamin D is essential to its utilization.

Calcium therapy undoubtedly relieves the muscular cramps that may occur during pregnancy. However, there is no evidence to assume that calcium administration prevents dental caries,³ a condition for the prevention and cure of which we must still rely on proper dental hygiene and care. Furthermore, there is some evidence to show that too much calcium and vitamin D may lead to early calcification in the fetal bones (osteosclerosis).⁴ As to the calcification of the teeth of the offspring, this, of course, is postnatal and does not depend on the ingestion, in addition to an adequate diet, of calcium and phosphorus by the mother.

It may be claimed safely that during pregnancy all calcium and phosphorus requirements are supplied by an adequate diet, containing these elements as well as the other dietary essentials. Certainly, any deficiency in these two elements, in the diet, may be corrected by the addition of milk, an easily assimilable source of these substances. The practice of instructing all pregnant patients to take one quart of milk a

¹Sherman, H. C.: *Chemistry of Food and Nutrition*, New York, 1911, Macmillan Co., p. 289.

²Bernheim, Alice E.: *Med. Woman's J.*, March, 1937.

³Report of Council of Pharmaceutics of American Dental Assoc., *J. Am. Dental Assn.* 23: 139, 1936.

⁴Brehm, Wayne: *Ohio State M. J.* 33: 990, 1937.

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filling the lower abdomen. There were no adhesions present. Both tubes were removed and the patient made an uneventful recovery, and is alive and well today. The microscopic section showed undoubted chronic tuberculous salpingitis. This case is presented to show what extensive lesions one may find without involvement of the peritoneum.

I should like to detail another case showing that a tremendous involvement of the pelvic structures may lie dormant for many years without producing symptoms, and then may relight under conditions of stress. About six months ago, a woman of twenty-eight years motored from Vancouver to Montreal with her husband, on their wedding trip. When she arrived in the vicinity of Montreal, she was brought to the hospital and exhibited signs of an acute abdomen. At operation a large mass in the right pelvis was disclosed, which later turned out to be an old tuberculosis, which had been primarily in the tubes, but had ruptured into the right broad ligament. The pelvis was cleared out, leaving a large cavity in the right broad ligament enervated with old tuberculous calcified material. Drainage was established from below.

The early history of this second patient was interesting, for it showed that she had had pelvic trouble when she was thirteen years of age, and was invalided at that time for a period of over a year. The process had quieted down, and she had been free from symptoms for fifteen years, carrying this large amount of tuberculous material in the broad ligament. The long trip, and the injuries of marriage, had brought about a secondary infection with an acute abdomen. The healing after operation was at first kindly, but two days before she was ready for discharge, a small sinus developed, which gradually enlarged and extended nearly the whole length of the incision. The discharge became very profuse, and a fistula developed. At the end of three months the patient died of inanition. She had overcome the secondary infection, but relighted the tuberculosis.

DR. KING (closing).—Unsuspected tuberculosis associated with other pelvic lesions is an interesting problem. In my series tuberculosis was found to complicate three fibromas, a large pseudomucinous cyst, and an endometriosis. A routine curettage disclosed two more cases of tuberculous endometritis.

I am entirely in favor of treatment without surgery if these patients could be diagnosed early enough. Unfortunately we cannot diagnose the early cases and the vast majority seem to require operation for the diagnosis.

Only rarely can sinuses be closed by surgery, but they yield readily to sanitarium treatment. The inexperienced surgeon will do repeated operations on these patients with sinuses. In one patient, a surgeon made three attempts to close a sinus, which healed after six weeks' sanitarium treatment.

The effect of sanitarium treatment is shown by the fact that the uncomplicated cases averaged a gain of 3.8 pounds per month and were soon discharged. The patients having extrapelvic tuberculous lesions do not have such rapid weight gain and require longer sanitarium care.

are not attempting to explain, and quite a few of our nonpregnant controls showed a complete loss of erythema at the same time. Thus the thirty-minute period was established for the observation. Before submitting the test to unknown cases, checks on 100 controls were made, thereby learning to read the reaction. It is yet 100 per cent in our hands.

Again the above-mentioned authors took a great deal of liberty in interpreting our statements. We did not recommend it in place of the Aschheim-Zondek, but did and still are proving it more sensitive, and still recommend it for its rapidity. Since our paper appeared, we have diagnosed and have operated upon twelve unruptured ectopics, and have reports of three more. Since the original paper, we have tried antuitrin-S that was considered by the manufacturer as impotent, and have found the same results as with the fresh product. This we feel is due to the fact that the active principle is apparently a protein; whether or not it carries with it activity, it remains of the same character, and is specific; therefore, it would be expected to show the same reaction in sensitized subjects. Because of the above assumption, it may never be (as suggested by Yerbury and Weisman) crystallized or synthetically produced. If crystallized, it certainly would be, as all other similar products have been, very irritating at the site of injection. Again, we defend the word new, for the substance which we used is new.

G. C. GILFILLAN, M.D.

*Dayton, Ohio,
April 21, 1937.*

day, especially during the last two trimesters of gestation, appears to be sound and to meet all requirements for calcium and phosphorus. Should it be necessary, because of dietary deficiencies, inability to drink milk, or lack of sunshine, to supply compounds of calcium and phosphorus and vitamin D, these must be administered with care, certainly in respect to vitamin D, as overtreatment may be as injurious as the deficiency itself.

H. J. Stander.

Correspondence

Photographic Records of the Cervix Uteri

To the Editor:

Sir,

With reference to the communication of Messrs Bruner, Rosebrook and Cushman in your recent issue (34: p. 1027, 1937), may I say that good photographs of the cervix have been published by Max Cheval (*J. Belge de Gynec. et D'Obst.*, July, 1914) and by Herbert R. Spencer and E. A. Barton ("A Speculum-Camera," *Proc. Roy. Soc. Med.* 9: p. 17, 1915-16). In the Speculum-Camera the speculum and the camera are combined, no separate stand being required as described in the other communications.

Yours truly,

HERBERT R. SPENCER, M.D.

London, Eng.

To the Editor:

In response to an article printed in *Medical Record*, March 3, 1937, written by Abner Weisman and Charles Yerbury, I would like to make the following statements:

First, the test is new, for a perusal of the work done by Porges and Pollatschek (with a hormonal substance) was done with a substance that necessarily would be very different from the antuitrin-S of 1936 and 1937. Loeser's work was done with the urine of pregnant women and not with the refined substance that we used. A letter from Loeser himself complimented us on our work, and also stated that he would carry out further work, when, and if he was able to obtain the product we were using, because with an unrefined substance, he felt that his results were accurate enough to justify further work with a refined product.

Dowell and Deutsche's work was a repetition of Porges and Pollatschek's experiments. So it does not count either for the same reason.

We are quite aware of the stand taken by the American Medical Association. They are also being misled by the early product of antuitary extract, instead of the derivatives of today.

As to the length of time for reading the reaction. Weisman and Yerbury erred in not reading the test in the thirty minutes. We did not stress six to eight hours in our report because we had made the same observations that they did, and proved to ourselves that the thirty-minute period was the time to record results. A great number of our nonpregnant patients showed an erythema at the end of one hour, which we

programs by the methods which are best suited to solving their varied problems. Each must take an inventory of its requirements and of the means available for meeting these requirements, and must supplement the existing resources with whatever other service and equipment is necessary to bridge the gaps in the program of complete maternal care.

We feel that the American Committee has made a definite contribution to developing programs of maternal care under the leadership of the medical profession. The formation of committees to lead and guide the programs of maternal care in every state and community should be the ultimate goal. This program is now well under way and to complete and carry out these plans requires only constant attention by those who are interested.

There should be closest cooperation between governmental, professional, and lay groups so that the best results may be obtained with the least friction and the minimum of antagonism, unnecessary duplication, and detrimental activities. This part of our program is well on its way and should continue further as its value is demonstrated.

In the past certain publications, such as the pamphlets on antepartum and delivery care, have emanated from our Committee. Also reprints of reports and articles have been circulated from time to time, usually without cost to the recipient.

There has just now appeared from The University of Chicago Press a booklet, bound either in cloth or in paper, entitled *Maternal Care*. This presents in concise and readable form the essential principles of antepartum, intrapartum, and postpartum care for the practitioner of obstetrics. It is of a size to be carried conveniently in one's coat pocket. The material was prepared largely by Drs. W. C. Danforth, G. W. Kosmak, R. L. DeNormandie, and myself. It was read by a number of the directors, and all the material and suggestions were carefully reviewed and edited. This booklet is being sold practically at cost and may be purchased from The University of Chicago Press at a price which varies with the type of binding and the number of copies purchased at any one time.

At the last annual meeting, acceptance was authorized of a proposal by Mead Johnson and Company to finance a "feature movie" for the education of the laity regarding the essentials of maternal care. The directors entered into such an arrangement; and a special committee consisting of Drs. E. D. Plass, J. R. McCord, A. J. Skeel, Philip F. Williams, and myself was appointed to carry the project through. We believe it marks a definite innovation and real progress in lay education regarding some of the fundamentals of life and will be released under certain conditions for lay education in states where the officials of the state medical societies approve of its presentation. It will be necessary to show it under proper conditions of visual and sound projection.

The American Committee on Maternal Welfare is now confronted with a large project of great importance which has been developed within the last eighteen months. I refer to the proposed "American Congress of Obstetrics and Gynecology." This idea was really started officially at the 1935 meeting of the Central Association of Obstetricians and Gynecologists by the appointment of a special committee consisting of Drs. E. D. Plass, Chairman, J. C. Litzenberg, and myself. The various national obstetric and gynecologic societies have been informed relative to this project, and formal action has been taken by some of them, including The Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, The American Gynecological Society, and The American Association of Obstetricians, Gynecologists and Abdominal Surgeons. Among the sectional organizations, The New England Obstetrical and Gynecological Society, The Texas Association of Obstetricians and Gynecologists, and The Pacific Coast Society of Obstetrics and

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

THE AMERICAN COMMITTEE ON MATERNAL WELFARE, INC.

ANNUAL MEETING, JUNE 9, 1937

Atlantic City, New Jersey

CHAIRMAN'S ADDRESS

FRED L. ADAIR, M.D., CHICAGO, ILL.

THE objectives of The American Committee on Maternal Welfare have been outlined at previous meetings and in publications which have appeared from time to time. Some of our chief efforts during the past few years have been to stimulate the interest of the medical profession and associated groups toward solving the problems associated with maternal care and forming state and local committees representing the medical profession to initiate and develop programs for securing adequate maternal care for all prospective mothers in their states and localities.

Such committees now exist in nearly all the states and territories and are, for the most part, official committees of the state and county medical societies. In some states temporary committees have been appointed by The American Committee on Maternal Welfare to function pending formal action by the state or territorial medical society. All of these committees have a sort of liaison with the parent American Committee, which has, and seeks to have, no control over the state and local committees but desires only to cooperate with them. The American Committee on Maternal Welfare desires to and wishes the subcommittees to work in harmony with all the governmental and other agencies which are interested in improving maternal care.

It realizes fully that there are many social and economic problems closely tied up with the dominant medical problems of maternal care; but it believes that proper medical and nursing care in the home, the out-patient clinic, the doctor's office, and the hospital are the most vital parts of maternal care.

It is further our opinion that the prevention of disability and deaths of mothers, fetuses, and newborn infants constitutes a unified problem and requires a single program for its solution.

We are also of the belief that maternal care cannot be divided into phases of antepartum, intrapartum, and postpartum care but insist that all these activities must be parts of a unified program.

Maternal care must be carried out intelligently, completely, and constantly for every prospective mother, no matter what her geographic, social, economic, or other status may be. The future of the human race depends upon such care being given to mothers and their infants.

Basic principles should be applied in a broad way, but the methods of application may differ. Various communities have differing needs depending upon many factors and facilities. It is our opinion that localities should work out their own

Surgeons, and the fulfillment of these is now required in all Approved Hospitals. These requirements have proved themselves to be sound and practical in their application. With minor adjustments, it is possible to apply them to any hospital caring for obstetric patients.

The following is a statement of each clause or requirement of the Minimum Standard for Obstetric Departments in Hospitals, with explanations when indicated and the present status of these requirements in a series of 1937 hospitals (1349 approved—588 not approved) as recently analyzed.

1. *Accommodation.*—*There shall be in all approved hospitals caring for obstetric patients a properly organized and equipped department of obstetrics, providing exclusive and adequate accommodation for mothers and the newborn.*

The foregoing requirement presupposes a definitely organized unit or service under competent administrative and professional supervision and direction. There must be a supervisor with special qualifications as an administrator and with a thorough knowledge of obstetric nursing technique and procedures. She must have special training, usually provided through acceptable postgraduate study and experience. Likewise, the professional supervision through a well-organized obstetric staff is most imperative. This can be best fulfilled through a well-organized clinical department or service within the medical staff with a chief or head of the department and associate assistant chiefs or heads as indicated by the size of the hospital and the amount of work. The chief or heads of the department should be held responsible for the professional policies and quality of the clinical or scientific work. Good organization of the medical staff, providing for control of the clinical work, is absolutely essential for the best results.

An analysis of 1937 hospitals under survey by the American College of Surgeons reveals the following results:

TABLE I. ORGANIZED DEPARTMENTS OF OBSTETRICS

All Hospitals Considered		1937
Acceptable	1702 (88%)	
Not acceptable	235 (12%)	
Approved Hospitals Considered		1349
Acceptable	1207 (89.5%)	
Not acceptable	142 (10.5%)	
Nonapproved Hospitals Considered		588
Acceptable	424 (72%)	
Not acceptable	164 (28%)	

Table I indicates satisfactory progress in developing proper departments of obstetrics in hospitals. There has been steady and most encouraging improvement in hospitals in this respect. Difficulty has been encountered in many of the smaller hospitals in providing satisfactory segregation of obstetric patients from other types in the hospital. It is most essential that such segregation be carried out as

TABLE II. SEGREGATION OF OBSTETRIC PATIENTS FROM OTHERS IN THE HOSPITAL

All Hospitals Considered		1937
Acceptable	1595 (82%)	
Not acceptable	342 (18%)	
Approved Hospitals Considered		1349
Acceptable	1207 (89.5%)	
Not acceptable	142 (10.5%)	
Nonapproved Hospitals Considered		588
Acceptable	388 (66%)	
Not acceptable	200 (34%)	

Gynecology have likewise expressed their interest and willingness to cooperate. The American Board of Obstetrics and Gynecology expressed its opinion that while it approved the plan as tentatively outlined, the sponsorship of such a movement was completely outside its established functions.

The American Committee on Maternal Welfare at its meeting in Kansas City, May 13, 1936, in view of the fact that its membership is representative of the various national and sectional specialty societies, agreed to promote and organize such a congress, provided the involved organizations desired it to act in this fashion.

The other sources of financial support will be from membership dues and from the sale of space for commercial exhibits.

According to the present outlook the Congress will have to be largely self-supporting, as there appear to be no other sources of revenue available at the present time.

The time of the meeting has been tentatively set for September, 1939, and the place in the midwest, though the city has not been definitely selected. The major purpose of the Congress will be to educate professional and lay groups, and its scope, the problems of human reproduction, chiefly as they affect the woman, and diseases of the female reproductive organs. The major objective will be the better understanding, the integration, and the co-ordination of the knowledge and activities of the various professional, institutional, governmental, and volunteer agencies which are interested in promoting the welfare of motherhood and of womanhood.

The development of the Congress will constitute the major activity of our Committee during the ensuing two years or more. The American Committee will, however, continue its activities in other lines as well as is possible with its limited finances, etc. If we accomplish a better understanding of our purposes, a better integration of our ideas, and better harmony and closer coordination of effort on the part of those individuals and agencies interested in improving conditions surrounding motherhood and womanhood, our efforts will not have been in vain.

THE PROGRAM OF THE AMERICAN COLLEGE OF SURGEONS FOR MATERNAL CARE IN GENERAL HOSPITALS

MALCOLM T. MACEachern, M.D., CHICAGO, ILL.

Associate Director of the American College of Surgeons

THE American College of Surgeons is deeply interested in improving the care of the obstetric patient, particularly in the general hospital. The College through its Hospital Standardization program aims directly at the proper organization, management, and functioning of the obstetric department so as to afford the patient the greatest measure of safety and efficient service not only during complications of pregnancy, but during labor and the puerperium. It is believed that if hospitals will conscientiously live up to the requirements as laid down by the American College of Surgeons, maternal morbidities and mortalities can be reduced and kept close to a minimum. It is toward this objective that the efforts of the College are being directed at the present time.

In 1928 the College informally set up certain fundamental principles or criteria which it was believed would tend to improve the care of maternity patients in hospitals. There were ten well-thought-out clauses in the Minimum Standard for Obstetric Departments in Hospitals, as promulgated by the American College of

It is quite apparent that though admirable progress has been made by hospitals in providing facilities for infected or suspicious cases much yet remains to be accomplished. It is frequently difficult for the small hospital to provide proper segregation of infected or potentially infected cases because of limited accommodations. Frequently this can be done only by using private rooms elsewhere than in the obstetric division.

It is also essential that provision be made for the segregation or isolation of the newborn when they develop skin rashes, bronchial conditions, or infection of any kind. In this respect, the survey reveals the results as shown in Table V.

3. *Facilities.*—*Adequate clinical laboratory, x-ray, and other facilities, under competent supervision, shall be provided for the diagnosis and treatment of obstetric patients.* Inasmuch as the obstetric service in the hospital depends on the general facilities of the institution, usually the necessary clinical laboratory, x-ray, and other services are readily available and offer a complete service to the obstetric patient. These services in general may be regarded as satisfactory and well provided.

4. *Administration.*—*The administration of the obstetric department shall be under the direction of a competent, registered nurse who has executive ability, who is especially trained in obstetric nursing, and who shall have an adequate number of assistants and other personnel to carry on efficiently the work of the department.* Emphasis has been placed on the need of having a competent graduate nurse in charge of the obstetric department. This presupposes a person with administrative ability and special training in the management of obstetric patients. She must be a good manager and a competent department head. The analysis of the series of hospitals used as a basis for this report is as shown in Table VI. In this analysis there was found a large and varying range of administrative ability.

TABLE VI. COMPETENT ADMINISTRATION OF OBSTETRIC DEPARTMENT

All Hospitals Considered		1937
Acceptable	1860 (96%)	
Not acceptable	77 (4%)	
Approved Hospitals Considered		1349
Acceptable	1333 (99%)	
Not acceptable	16 (1%)	
Nonapproved Hospitals Considered		588
Acceptable	527 (90%)	
Not acceptable	61 (10%)	

5. *Supervision.*—*The obstetric division of the medical staff shall be so organized as to exercise adequate control over the clinical work in that department, such organization to include a chief or head of the department or service who shall be responsible for the general supervision of the obstetric work of the hospital.* It is most important that all the obstetric work of the hospital be under competent supervision at all times. This presupposes good medical staff organization. It is recognized that in most hospitals obstetrics is practiced largely by general practitioners and the work is not limited to qualified obstetricians. In the survey, it was found that the obstetric staff was organized, although frequently too loosely and without sufficient positive supervision over the actual work. Active supervision by the chief or head of the department or service must extend to all types of patients rather than to the ward patients only. Sometimes this supervision is delegated to a committee. Finally, one may say that while better control and supervision of the obstetric work in hospitals is evident, there is much need for greater achievement in this respect. Better medical staff organization is widely indicated.

6. *Records.*—*Accurate and complete medical records complying with the required standard shall be provided for all patients admitted to the obstetric department.* Adequate obstetric records present a real difficulty in many hospitals. Too often

a safeguard against infection. Likewise, there must be complete segregation of nursing personnel. Table III indicates how far this is being accomplished in the series of hospitals considered.

TABLE III. SEGREGATION OF NURSING PERSONNEL

All Hospitals Considered		1937
Acceptable	1308 (68%)	
Not acceptable	629 (32%)	
Approved Hospitals Considered		1349
Acceptable	1107 (82%)	
Not acceptable	242 (18%)	
Nonapproved Hospitals Considered		588
Acceptable	201 (34%)	
Not acceptable	387 (66%)	

2. *Segregation or Isolation of Infected Mothers.*—*Special accommodations and facilities shall be available for all cases of infections, elevated temperatures, or any other conditions inimical to the safety and welfare of the patients in the obstetric division.*

The patient with a temperature, sore throat, puslike discharge, or infection of any nature, is a menace to other patients in the obstetric division and should be segregated immediately in order not to infect other patients. To this end, so far as practical and possible, all hospitals caring for obstetric patients are urged to set aside a special, properly arranged, self-contained unit, apart from the obstetric division. Any cases which show infection of any kind should not be placed on surgical or gynecologic wards where there are open wounds which might be readily infected. Adequate segregation or isolation must be promptly carried out so as to avoid the spreading of infection from one patient to another. In respect to this aspect, the analysis of the same group of hospitals already referred to reveals the results as shown in Table IV.

TABLE IV. SEGREGATION OR ISOLATION OF INFECTED MOTHERS

All Hospitals Considered		1937
Acceptable	1852 (95.6%)	
Not acceptable	85 (4.4%)	
Approved Hospitals Considered		1349
Acceptable	1319 (97.7%)	
Not acceptable	30 (2.3%)	
Nonapproved Hospitals Considered		588
Acceptable	533 (90.6%)	
Not acceptable	55 (9.4%)	

TABLE V. FACILITIES FOR THE ISOLATION OR SEGREGATION OF THE NEWBORN WITH INFECTION

All Hospitals Considered		1937
Acceptable	1785 (92.2%)	
Not acceptable	152 (7.8%)	
Approved Hospitals Considered		1349
Acceptable	1252 (92.80%)	
Not acceptable	97 (7.20%)	
Nonapproved Hospitals Considered		588
Acceptable	533 (90.64%)	
Not acceptable	55 (9.36%)	

8. *Morbidity.*—*All hospitals caring for obstetric patients shall adopt a morbidity standard by which they can better control morbidities.* It was found in the survey that only a limited number of hospitals had actually adopted and were using a morbidity standard. It is evident that insufficient attention has been given to this matter. All hospitals should be urged to adopt one of the recognized morbidity standards, particularly the one formulated and recommended by the American Committee on Maternal Welfare. It is difficult to measure the efficiency of the medical and nursing services and stimulate regulation and investigation of unfavorable conditions without the use of such a standard. Further, the information gained thereby provides subject matter for discussion in the review and analysis of the work of the obstetric department each month.

9. *Conferences.*—*A thorough review and analysis of the obstetric work in the hospital shall be made at least monthly, with particular attention given to mortalities and morbidities or any of the results not up to the required standard.*

Systematic and thorough review and analysis of the work in the obstetric department of the hospital is lacking in a number of hospitals. While the survey shows a review and analysis is attempted in the majority of hospitals surveyed, yet the analysis is not as thorough and complete as it should be nor is there adequate consideration of morbidities. Possibly in the general staff conference, the work of the obstetric division may be overlooked to a certain extent. It is for this reason that the departmental conference for the review and analysis of the obstetric work should be encouraged.

TABLE X. ANALYSIS OF OBSTETRIC WORK

All Hospitals Considered		1937
Acceptable	704 (36.3%)	
Not acceptable	1233 (63.7%)	
Approved Hospitals Considered		1349
Acceptable	625 (46.3%)	
Not acceptable	724 (53.7%)	
Nonapproved Hospitals Considered		588
Acceptable	79 (13.4%)	
Not acceptable	509 (86.6%)	

Table X gives the results of the survey in respect to the obstetric work in the hospitals under survey. From the above statistics it is apparent that there still exists need for improving the review and analysis of the obstetric work in hospitals with particular emphasis on morbidities and mortalities, and so far as possible and practicable such a review and analysis can best be carried on through the departmental conference.

10. *Training.*—*Opportunity shall be afforded student nurses in hospitals having a school of nursing for adequate theoretical instruction and practical experience in prenatal work, observation of the patient in labor, delivery room technique and postpartum care of the mother, as well as the proper nursing care of the newborn.*

Usually the training of student nurses in obstetric work was found to be fairly well done, although frequently the period of time allowed for experience in this division was too limited. It would appear to be most difficult to offer student nurses adequate essential training and experience in this work under a period of four months at least. In many instances this is not more than three months, and in some instances it is less. It would also appear to be advisable that the student nurse complete her work in the surgical department before being assigned to the obstetric division. The teaching and training of the student nurse, as well as that of the interne, could be greatly enhanced by more individual instruction at the bedside and group demonstrations on patients. Careful instruction and supervised

these are lacking in sufficient data, particularly in respect to the pregnancy or pre-natal record, pelvic measurements, and indications for operative interference. The forms for record taking in connection with obstetric patients are generally very good. The survey of hospitals in respect to obstetric records reveals the status of this phase

TABLE VII. ADEQUATE OBSTETRIC RECORDS

All Hospitals Considered		1937
Acceptable	1035 (53%)	
Not acceptable	902 (47%)	
Approved Hospitals Considered		1349
Acceptable	908 (67.42%)	
Not acceptable	441 (32.58%)	
Nonapproved Hospitals		588
Acceptable	127 (21.59%)	
Not acceptable	461 (78.41%)	

of the work as shown in Table VII. An analysis of the obstetric records of the same group of hospitals for recorded indications of operations reveals the conditions as shown in Table VIII. It is quite evident that adequate obstetric records are still

TABLE VIII. RECORDED INDICATIONS FOR OPERATIVE OBSTETRICS

All Hospitals Considered		1937
Acceptable	787 (46%)	
Not acceptable	1150 (54%)	
Approved Hospitals Considered		1349
Acceptable	672 (42.40%)	
Not acceptable	677 (57.60%)	
Nonapproved Hospitals Considered		588
Acceptable	115 (19.55%)	
Not acceptable	473 (80.45%)	

lacking in many hospitals, and special efforts should be directed in this respect. More interest and cooperation are required on the part of the medical staffs of hospitals; and the management, too, must realize its responsibility. Continuous efforts are required in order that obstetrical records may reach acceptable standards.

7. Consultations.—Major obstetric procedures shall be carried out only after consultations and indications for interference are recorded on the patient's clinical record, exceptions being made when the attending physician is a qualified obstetrician and in case of emergency when time does not permit.

It is apparent that consultations are increasing. Frequently, however, the consultant is not a qualified obstetrician and this may make the consultation of little value. Such consultations should be with qualified obstetricians. The results of the survey in respect to this aspect of obstetric work are as shown in Table IX. Better enforcement of the rule or policy of recorded consultations of an acceptable type is desired.

TABLE IX. CONSULTATIONS

All Hospitals Considered		1937
Acceptable	675 (34.85%)	
Not acceptable	1262 (65.15%)	
Approved Hospitals Considered		1349
Acceptable	584 (43.29%)	
Not acceptable	765 (56.71%)	
Nonapproved Hospitals Considered		588
Acceptable	91 (15.47%)	
Not acceptable	497 (84.53%)	

Education of Mothers Before Leaving Hospital.—Unfortunately too many mothers leave the hospital without adequate instruction as to their own care or that of their babies. Too often the splendid results obtained in the hospital are for naught because of the ignorance of the new mother as to her own hygiene and diet and the proper care of the baby as to feeding, bathing, clothing, fresh air, etc. The supervisor of the obstetric department can do a great deal to remedy this condition by seeing that each mother, prior to discharge, is carefully instructed so that after her return home a proper regimen can be carried out which will assure a healthy mother and child. Every hospital should be equipped to carry on this valuable service.

CONCLUSION

The comments and tables submitted are not to be considered hypercritical of the care of obstetric patients in general hospitals, but rather as a basis for constructive thought and action in encouraging and stimulating every hospital to put into effect such conditions as will insure full compliance with the requirements as laid down by the American College of Surgeons. Indeed, if a graph of progress could be indicated during the period Hospital Standardization has been carried on, vast improvement could be noted in every phase of the work described in the text of this presentation. Conditions surrounding the care of the obstetric patient have improved immensely as well as other phases of hospital work during the same period.

The problem now is one of education, not only of hospital executives and governing boards of hospitals, but also of members of medical staffs who must share some of the responsibility for the proper care of the patient. Governing boards, hospital executives, and medical staffs must unitedly and with the closest cooperation put forth every possible effort to meet the requirements as stated and see that they are carried out to the fullest extent. When this is done, greater improvements may be expected in the obstetric service in every hospital; and then morbidities and mortalities will be further reduced.

OBSERVATIONS ON THE TEACHING OF OBSTETRICS

H. G. WEISKOTTEN, M.D., SYRACUSE, N. Y.

(*Dean of the College of Medicine, Syracuse University*)

IN DISCUSSING the teaching of any particular subject in the undergraduate medical curriculum, it is important to bear in mind the recognized objectives and some of the general trends involving the curriculum as a whole. The principal objectives of undergraduate medical education have been stated by Dr. Fred L. Adair as follows: "The laying of the foundations for a knowledge of medicine on which subsequent structures can be built for general or special practice and for teaching or research and for public health activities." In many colleges there is evident a distinct effort to make the entire curriculum a coordinated whole directed toward the laying of such a sound foundation for a career in the field of medicine.

For a number of years there has been a tendency to emphasize clinical training in the undergraduate course. The fundamental sciences are being taught with more emphasis on their clinical implications. Correlation clinics in connection with the teaching of these subjects are becoming recognized features of the curriculum. In most of our more progressive medical schools the students are introduced to the clinical subjects in the second year, and the third and fourth years are devoted almost entirely to clinical work in the hospital and the outpatient department.

experience in observing the patient in labor, and accuracy of recording observations, are most desirable. Nurses' records as a whole were fairly good, but in many instances could be improved in the details mentioned.

It was noted in the survey that many institutions found it most difficult to obtain postgraduate training for their nurses to fit them for executive positions. There appears to be a general lack of good postgraduate training opportunities for those desirous of further advancement and wishing to prepare themselves for administrative position. Very few hospitals offer well-organized, desirable courses in this regard. More postgraduate courses of a desirable standard are greatly needed.

During the survey certain other observations were made and certain conclusions arrived at. These were as follows:

Pelvic Measurements.—The practice of carefully measuring obstetric patients prior to the eighth month, or even at any time, appears to be sadly neglected. Regardless of the merits or demerits of pelvimetry, it should not be neglected and, when properly done, may result in lessening the ever-increasing amount of operative obstetrics as noted in recent years. The members of the medical profession who practice obstetrics are in great measure negligent about this important phase of diagnosis as to the relation between the size of the child and the pelvic outlet. A more effective enforcement of the rule that all obstetric patients should be measured, would do much to improve obstetric results, particularly in cases of contracted pelvis.

Incidence of Cesarean Section.—An incomplete analysis of the hospitals under survey indicated the following results:

All Hospitals Considered	168,052 deliveries
Total Number Cesarean Sections	5,445
Percentage	3.2
Approved Hospitals Considered	159,887 deliveries
Total Number Cesarean Sections	5,027
Percentage	3
Nonapproved Hospitals Considered	8,165 deliveries
Total Number Cesarean Sections	418
Percentage	5

The lack of recorded indications before cesarean section was noted in a large percentage of cases. Not infrequently consultations were lacking. In this tabulation, it was interesting to note the wide variation in the incidence of cesarean sections in individual hospitals, this varying from zero to 19 per cent. Better control of this phase of obstetric work is indicated.

Medical Care of the Newborn.—A study was made as to who took care of the baby after birth and the following was noted:

Obstetrician	1665
Pediatrician	207
Obstetrician and Pediatrician	32
Ward Service	34

It is quite evident there is no uniform method of caring for the infant or newborn, but this varies considerably. There does appear to be a distinct tendency in the larger and better organized obstetric clinics or departments to put the newborn on the pediatric service, but this is not yet universal by any means.

colleges in the United States teaching obstetrics have such combined departments of gynecology and obstetrics, in many instances this combination is entirely artificial and apparently is merely a paper set-up in response to a popular trend.

The didactic teaching is begun in the second year in 29 of the colleges. Most of the colleges devote an adequate amount of time to the didactic teaching, and a number, what would appear to be an unwarrantedly large amount of time.

All of the colleges offer their students some experience in prenatal examinations and prenatal care. In too many instances this aspect of the teaching is entirely inadequate, unsystematic, and haphazard. The number of prenatal clinics attended by students varies from two to thirty or more. In some colleges students have their prenatal clinic experience after they have had their experience in deliveries.

The number of deliveries observed by students varies from 2 to 100. All too frequently these involve students in large groups observing deliveries in the hospital amphitheatre.

The number of actual deliveries by students varies from none up to 50 or more. In 16 of the schools the students have less than 5 deliveries each. In 34 colleges each student has at least one delivery in the teaching hospital. The complete availability of an adequate amount of clinical material under conditions which permit a high standard of training and experience for undergraduates and internes is apparently becoming a very serious problem in connection with the teaching of obstetrics.

Forty-five colleges have home delivery services available for student training. Sixteen of these provide no regular supervision of student deliveries. In 10 colleges students are supervised by an interne and in 13 by a resident. Only 6 colleges offer regular supervision of student deliveries in the home by a member of the departmental staff above the rank of resident.

Most of the colleges are largely dependent upon home deliveries for the actual experience of the students in delivery technic. There is occurring a marked decrease in the number of deliveries in the home. Statistics indicate an increase of approximately 70,000 births in the hospitals of the United States during 1936 as compared with 1935. In many localities practicing physicians are being paid from government funds for the delivery of the indigent in their homes. Several of the colleges reported that their teaching home delivery services had been practically wiped out by the initiation of such programs.

Fifteen colleges have no required supervised hospital clerkships in obstetrics, involving the assignment of cases to be followed through labor.

Although questionnaire data indicated otherwise, only 22 colleges reported systematic manikin practice by the students. I found a great divergence of opinion on the part of the professors of obstetrics as to the value of manikin practice. Some feel that it is an essential and very valuable feature of the undergraduate course while a few feel that it is practically worthless.

I will now endeavor to outline briefly my personal reactions to the teaching of obstetrics in this country.

Obstetrics is but one element in what should be a well-coordinated curriculum. Much of the knowledge and training essential to obstetrics is taught in the departments of anatomy, physiology, bacteriology, pathology, medicine, and surgery. Training in proper methods of work and the development of the scientific viewpoint must be a part and parcel of every course given in the school.

My own feeling is that the number of didactic hours devoted to obstetrics matters little so long as there is adequate time to cover the essentials systematically. My chief interest is in the competence, interest, and viewpoint of the teacher to whom these hours are assigned. All too frequently the book is "cut" and parceled out

There is no longer an effort to cover fully all subjects in didactic exercises. Emphasis is rather placed on a thorough understanding of the principles of the fundamental sciences in their relations to clinical medicine, the development of various technics in the examination of patients, the acquiring of proper methods of work, the development of the scientific viewpoint, and the following of the progress of disease together with a study of the effects of certain therapeutic procedures. Increasing emphasis is being placed upon the preventive and the social and community aspects of medicine.

The fundamental nature and the incompleteness of the undergraduate course as far as preparation for the practice of medicine is concerned are fully recognized by both medical faculties and graduates. Although required by but few medical colleges and only a few state licensing boards, more than 99 per cent of all graduates of the medical colleges of this country are serving internships after graduation and before beginning practice. Thus, practically all graduates acquire considerable clinical experience beyond the formal medical course. This situation emphasizes the importance of the internship as an integral part of medical education.

The objectives to be attained in connection with the undergraduate teaching of obstetrics will depend upon the subsequent experience a student is to have before beginning practice and the responsibilities which will be his as a practitioner. Certainly every graduate before beginning the general practice of medicine should have adequate knowledge and training in preconceptional, prenatal, delivery, and post-partum care to justify him in assuming the responsibilities involved in ordinary safe obstetric care. This should be one of the ultimate objectives and responsibilities of those responsible for medical education.

Although as previously stated more than 99 per cent of our graduates serve internships before beginning practice, only 78 per cent serve general or rotating internships, the remainder serving in specialized or so-called "mixed" internships. Many of this latter group have no obstetric training whatever in connection with their internships.

Recent studies indicate that practically one-tenth of the graduates entering upon the general practice of medicine have served such straight or mixed internships and have had no other graduate training before entering practice.

Let us add to this picture the fact that more than 25 per cent of all the graduates of the medical colleges in this country are today locating in communities of less than 5,000 population and an additional 6 per cent are locating in communities of from 5,000 to 10,000 population.

Regardless of the feeling which any group may have in regard to the practice of obstetrics being a specialty, these data give us some idea as to the usual internship training in obstetrics and the responsibilities graduates are called upon to assume as they enter upon the practice of medicine.

It is also on the basis of such data that the medical colleges must recognize their objectives and responsibilities in the teaching of obstetrics.

I will now discuss briefly the present status of obstetric teaching in the medical colleges of this country as observed in connection with my visits to the colleges as a part of the recently completed survey of medical education.

At the very beginning of the survey it was recognized that it would be impossible to analyze and evaluate accurately all of the details of the various elements of the undergraduate curriculum. However, certain fundamental facts could be definitely determined, and in general it was possible to formulate a fairly clear picture of the courses being offered.

During recent years there has been considerable discussion in regard to combining gynecology and obstetrics in a single department. Although 38 of the 67

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Complications of Pregnancy With Disease

Brindeau, Kowilsky, R., and Kowilsky, S.: Pulmonary Tuberculosis in the Pregnant Woman, *Presse méd.* 93: 1865, 1935.

The obstetrician should be guided by the findings and conclusions of the tuberculosis specialist upon whom rests the major burden of the responsibility for the care of the tuberculous pregnant woman.

In evaluating the physical status of the patient they greatly stress a biologic reaction or tendency which they define as the "intensity of the casifying process." According to the latter there are four types: (1) Acute, (2) subacute, (3) chronic fibroulcerative, and (4) discrete fibroulcerative.

1. The acute forms with rapid evolution, high fevers and marked caseous tendency are hopeless from the standpoint of medical or obstetric therapeutics (collapse therapy or abortion).

2. For the other forms, artificial pneumothorax, uni- or bilateral, or therapeutic abortion, or a judicious combination of both procedures may be indicated.

3. Pregnancy exerts, during the first three months and especially in the post-partum period, a definite, aggravating influence upon the evolution of the tuberculous process. This effect of exacerbation is noted also in extrapulmonary tuberculous lesions, and even in nontuberculous infections.

ARNOLD GOLDBERGER.

Frisch, A. V.: Pulmonary Tuberculosis and Pregnancy, *Wien. klin. Wchnschr.* 42: 1287, 1936.

That pulmonary tuberculosis may occasionally be unfavorably influenced by pregnancy is well known. Whether it always justifies interruption of pregnancy is questionable. In the milder, more benign cases of pulmonary tuberculosis, termination of pregnancy is not necessary. In the more severe types such as the dense fibrous diffuse tuberculosis, interruption of pregnancy may be recommended especially where there is hemoptysis, fever and tubercle bacilli in the sputum. In a follow-up of 100 cases of pregnancy complicated with tuberculosis, not one case of tuberculosis was unfavorably influenced by the pregnancy. In a severe case the patient went to term but died later of tuberculosis. The author recommends collapse therapy also during pregnancy.

W. B. SERBIN.

Peters and Davenport: Pregnancy and Parturition During the Course of Bilateral Artificial Pneumothorax, *Am. Rev. Tuberc.* 35: 71, 1937.

The writers present a comprehensive review of pneumothorax therapy done on pregnant women. The coincidence of bilateral artificial pneumothorax obviously is of

to a large group of young instructors, each to cover his section as best he may. Frequently there seems to be a tendency for these young teachers to emphasize the teaching of operative obstetrics, as they find it more interesting in connection with their own individual development as obstetricians.

One of the main objectives of the didactic hours should be to point out and clarify the essentials without which a student cannot hope to have a clear understanding of the subject. They must also serve as a stimulus for further independent study by the student. And may I emphasize at this point the importance of "tuning" the curriculum in any particular college to its average student. There is little to worry about in connection with the outstanding student.

Obstetric examinations, including abdominal palpation and external and internal pelvimetry, are frequently taught in a haphazard manner while the teaching of the rest of physical diagnosis is highly systematized. There are more definite and usually more satisfactory opportunities for teaching obstetric examinations than there are for teaching many of the other aspects of physical diagnosis. Furthermore, as a graduate enters practice there frequently will be much more at stake in connection with the making of an obstetric examination.

With the disagreement among obstetricians in regard to the value of manikin practice, I will not disclose my reaction to it further than to state that I believe that one of its functions should be to impress upon the student the difficulties of operative obstetrics rather than to teach operative obstetrics.

During the course of the survey I developed some very strong reactions to the delivery experience offered medical students. Granting the serious shortage of available clinical cases merely emphasizes the importance of using to the best possible advantage the cases which are available for teaching both in the hospital and in the home. This suggests that each student delivery should be supervised by a competent teacher. One such delivery surely means more to the average student than a dozen unsupervised deliveries.

To me it appears that, granting the required minimum of course content, it is much more important how well the subject is taught than how much it is taught.

Few schools can hope to give their average undergraduate training and experience in the handling of the various complications of labor but all can teach him the importance of their early recognition so that the services of a specialist can be secured.

Every college should impress upon its students that no graduate has the right to enter general practice until he is competent to manage a normal obstetric case and competent to recognize the abnormal in connection with which he will need experienced assistance.

Personally I have little confidence in detailed requirements for a certain amount of graduate experience in obstetrics set up by state boards of licensure, serving in any material way to improve the practice of obstetrics.

The development of a proper viewpoint on the part of medical college graduates and the creation of a public demand for safe maternity care will accomplish much more than any legal requirements.

As far as the medical curriculum is concerned the four essentials to a satisfactory undergraduate course in obstetrics are ample facilities, a reasonable allotment of time, capable teachers, and the maintenance of high standards by the institution as a whole.

is used he counsels the employment of either sterile water or a 1 to 2 per cent solution of argyrol, and deprecates the use of the more irritating silver nitrate or higher concentrations of argyrol.

Vaccine-therapy has not yielded any demonstrable effects. Chemical therapy is generally exhibited as intravenous methenamine, or, better, as intravenous mercurochrome. The former is not employed when cystitis is present, and the latter only in doses of 30 mg. during the febrile phases of infection.

THOMAS R. GOETHALS.

Soule, S. D.: Syphilis and Pregnancy, J. Missouri M. A. 34: 84, 1937.

Every pregnant woman should have a blood Wassermann taken at the time of her first visit. Intensive antisyphilitic treatment should be instituted as soon as a diagnosis of syphilis has been made. When the diagnosis is doubtful, treatment should be advised as a prophylactic measure. The patient should understand her condition clearly. Her cooperation is absolutely essential to successful completion of an efficient and adequate course of therapy. Treatment consists of weekly arsphenamine or neoarsphenamine injections in series of at least ten treatments. The last few intravenous injections are overlapped with intramuscular bismuth injections, which are then continued for six to ten weeks, followed by a return to arsphenamine. When time does not permit an adequate course of treatment, the drug of choice is arsphenamine, given at weekly intervals, for the remaining duration of pregnancy. Treatment is continuous without rest periods from the time of diagnosis until delivery. An intensive follow-up of the newborn should be instituted for at least three months and preferably for a year. A centralized unit, where prenatal observation is made at the same time that treatment is administered, has proved satisfactory. Attendance has been better and the amount of treatment administered per patient has been greater. Under this care patients who receive a moderate amount of treatment have almost a 95 per cent opportunity of delivering a living normal, nonsyphilitic child.

J. THORNWELL WITHERSPOON.

Castallo, M. A., and Rakoff, E. E.: An Analysis of 259 Cases of Syphilis Complicating Pregnancy, Penn. M. J. 39: 24, 1935.

Serologically negative pregnant women should always be given antisyphilitic therapy when there is a past history suggestive of syphilis such as repeated premature deliveries, macerated fetuses, stillbirths, when there has been a previous positive Wassermann reaction, when the paternal Wassermann reaction is positive, and when previous clinical signs of the disease have been elicited.

The authors emphasize that every syphilitic mother, irrespective of the amount of treatment she has received in the past and regardless of her physical condition or the status of her present Wassermann reaction, should receive early and adequate antisyphilitic therapy during each pregnancy to insure the birth of a live, nonsyphilitic baby. They agree that the pregnant syphilitic woman tolerates treatment much better than the nonpregnant, and that complications following treatment are only one fifth as frequent as after the treatment of a nonpregnant woman. The dose of the drug, however, should be less than that administered to the nonpregnant individual.

The authors found, as is usually the case in a large clinic, that invariably the percentage of syphilitic negroes is considerably higher (usually 3 to 5 times) than for white women. The negro, however, tolerates syphilis much better, both as to the outcome of the pregnancy and clinical relapse, than does the white woman.

rather rare occurrence. Probably not more than the 16 cases (briefly quoted) so far have been reported. A new instance is described in detail. Among other conclusions the writers mention the necessity of revision of prevalent views concerning proper procedure when a pregnancy starts in the course of unilateral or bilateral pneumothorax. There is no justification for interruption either of pregnancy or treatment. Indeed, often pneumothorax therapy is clearly indicated when a phthisical patient becomes pregnant or when a pulmonary tuberculosis develops in a pregnant woman. Instead of thinking first of interruption we must think first of proper treatment of the tuberculosis. Of course, pneumothorax at times is entirely ineffective but so is abortion.

HUGO EHRENFEST.

Praloran, Luigi: Collapse Therapy in Pregnancy, *Clinica ostet.* 15: 634, 1936.

The author thoroughly reviews the history of collapse therapy, citing the first case of pulmonary tuberculosis during pregnancy cured by Forlanini (1910) with the pneumothorax treatment.

He reports 80 cases of pregnant women placed on collapse therapy, treated as follows: Unilateral pneumothorax, 50 women; bilateral pneumothorax, 2; phrenectomy and pneumothorax, 11; phrenectomy, 14; Jacobaens operation and pneumothorax, 1; anterolateral thoracoplasty, 1; and apical collapse with phrenectomy, 1.

Up to date the results are as follows: Improved, 63 to 78.7 per cent; not improved, 12 to 15 per cent; stationary, 3 to 3.8 per cent, and dead, 2 to 2.5 per cent.

The effect upon the duration of pregnancy was as follows: Delivered at term, 72 to 90 per cent; delivered prematurely, 6 to 7.5 per cent; aborted 2 to 2.5 per cent.

The author concludes that collapse therapy is undoubtedly efficacious during pregnancy.

AUGUST F. DARO.

Lissack, E.: Pregnancies After Nephrectomy for Tuberculosis, *J. Missouri M. A.* 33: 450, 1935.

In general, tuberculosis of the kidney precludes pregnancy. The author reports a patient who was delivered of four living and healthy children after nephrectomy for tuberculosis. He concludes that nephrectomy is not a contraindication to pregnancy and that patients showing no abnormalities may be allowed to continue pregnancy under close observation.

J. THORNWELL WITHERSPOON.

Compan, V.: Influence of Pregnancy on Renal Excretion, *Rev. med. de Barcelona* 25: 351, 1936.

Alterations in renal excretion in pregnancy are due to a variety of causes. Undoubtedly the endocrine changes which cause excretion of lutein and prolan in the urine have something to do with these alterations, and may eventually be proved to have some effect in predisposing to infection. That mechanical changes are important is evident, as the increasing development of the uterus causes anatomic alterations in the pelvic ureter, and the enlarged uterus itself may cause sufficient pressure on the ureters at the pelvic brim to obstruct the passage of a catheter above this level.

In the treatment of pyelitis of pregnancy the author is an exponent of the indwelling ureteral catheter, which he often leaves in situ for twelve days or more, relying on this means to secure adequate drainage of the infected renal pelvis. If pelvic lavage

restlessness, nausea and vomiting are followed usually by delirium, semistupor, and finally coma. About one-half of this series had convulsions which became generalized.

The blood pressure and urinary findings are not altered much initially. Leucocytosis is frequent.

The brain lesion is a diapedesis of red cells around dilated capillaries and is concentrated in the white substance, yet often scattered in the grey matter. The more frequent sites are the corpus callosum, caudate and lenticular nuclei, pons and medulla.

The recommendations are: not more than 0.3 gm. of neoarsphenamine weekly as overdosage is the greatest danger; pregnant women are more susceptible and thus must be carefully watched while under treatment: careful observation of any of the above symptoms coming on about two days after any of the first few injections; and large doses of adrenalin if the disease develops and spinal drainage if cerebral edema is present.

H. CLOSE HESSELTINE.

Dick, W.: Is Transmission to Offspring Possible in a Case of Lymphogranuloma Inguinale? Med. klin. 32: 319, 1936.

Women with the late forms of inguinal lymphogranuloma are often sterile but occasionally give birth to mature infants. In the latter case the fate of the offspring is of interest. The author reports two cases. One concerns a woman with a positive Frei reaction and rectal stricture, who became pregnant and gave birth to a normally developed infant, who had a positive reaction when subjected to a Frei test two weeks after birth. Moreover, at five months the test was again positive. The second case cited by the author concerns a girl, aged fourteen, the daughter of a woman who had died following an attempt to dilate a rectal stricture, the latter being doubtless the result of an inguinal lymphogranuloma. The daughter had complained of rectal disturbances for a number of years; Frei's test was positive, indicating that her rectal disturbances were due to inguinal lymphogranuloma. In this case three modes of transmission were possible: intrauterine infection, infection during the process of birth, and infection after birth by contact with the mother. The author points out that intrauterine transmission seems likely in view of the fact that in adults the Frei test does not become positive until several weeks after the infection and that the nursing baby had a positive Frei test two weeks after birth.

J. P. GREENHILL.

Roxas, Katigbak, and Leyva: Neurologic Disturbances in Pregnancy and Their Relation to the Calcium and Phosphorus Balance in the Blood, Philippine Island M. A. 16: 535, 1936.

Seventy-eight cases were studied clinically with serum analysis for calcium and phosphorus. Hypocalcemia was found associated with neurologic disturbances in 86.2 per cent of the cases. The blood range in beriberi was also determined in 6 pregnant and 17 nonpregnant women and this may serve as a differential point.

The author contends the cases are insufficient in number to merit anything but a tentative conclusion. He tried to show a relationship between the neurologic disturbances and the calcium concentration in the blood. The condition is frequently met with in the dispensary class. The relation of beriberi merits further study in view of its disastrous effect on the mother.

C. O. MALAND.

In the authors' series of 259 cases, neoarsphenamine was administered to 120, acetylarsan to 57, 8 were treated by private physicians while 65 patients received no treatment at all. Twelve patients received combined therapy.

Among the 65 untreated syphilitic patients there were 20 per cent stillbirths and 10.8 per cent miscarriages, whereas in 80 patients receiving 6 or more treatments there were 2.5 per cent stillbirths and no miscarriages. In 37 patients in whom treatment was started before the sixth month there were no stillbirths and 5.4 per cent miscarriages. The results for the entire group of syphilitic pregnant women, treated and untreated, showed 8.3 per cent stillbirths and 3.5 per cent miscarriages.

The authors' statistics further showed that 13.1 per cent of the patients with a positive Wassermann reaction who received no treatment and had live births, lost their babies before discharge from the hospital. Among the group of patients who had treatment prior to the sixth month of pregnancy, only 2.9 per cent of the babies died before the mothers left the hospital.

In the 259 cases reviewed there was one maternal death from septicemia following cesarean section. There were no deaths attributable to the antisyphilitic treatment. There were, however, three cases of clinically evident complications directly attributable to the treatment. Two of the patients presented an arsenical hepatitis, while the third developed an arsenical dermatitis. All responded well to treatment. In addition to these there were occasional cases in which the patients experienced temporary gastrointestinal disturbances, syncope, and nitritoid reactions.

It is concluded that the pregnant woman tolerates antisyphilitic treatment well, and the results for both the mother and her unborn child justify its practice.

J. P. GREENHILL.

Woods, E. B.: Complications of the Treatment of Syphilis in Pregnancy. Report of Three Cases of Arsenical Encephalitis Complicating Such Treatment, J. Med. A. Georgia 25: 23, 1936.

Woods calls attention to the possible complications in the treatment of syphilis in pregnancy. Emphasis is placed upon the possible confusion of eclampsia and arsenical encephalitis. Careful watching and daily contact with these patients is necessary in order that prodromal symptoms and minor complications which indicate sensitivity may be recognized, for the early recognition of these with cessation of antisyphilitic treatment is the only effective therapy in such complications. Even though there is some danger of reaction from the medicaments used, the overwhelming benefit derived in the majority of pregnant women, together with the responsibility to the unborn child, leaves to the conscientious medical practitioner no choice.

J. P. GREENHILL.

Cormia, Frank E.: Hemorrhagic Encephalitis From Neoarsphenamine in Pregnancy, Canad. M. A. J. 35: 610, 1936.

The author reports a fatal hemorrhagic encephalitis occurring in a pregnant patient from neoarsphenamine and then reviews the 135 reported cases. There are 34 known pregnant patients for the review. In general the reaction comes on within five to seven days after 2 or 3 injections of 0.45 gm. of neoarsphenamine (or equivalent). It appears that the incidence runs parallel with the time of larger dosages. The use of heavy metals seems to have little influence. The common prodromal symptoms of fever, headache or generalized body pains, dizziness,

The greatest number of mental derangements occurred in primiparas. In these the chances of recovery are more favorable than when present in the second or third pregnancy. In addition to the childbearing as a cause of the breakdown, a number of other factors were found present which appeared to play a part in the development of the psychosis.

F. L. ADAIR AND S. A. PEARL.

Wong, Amos: A Case of Insomnia in Pregnancy, *Chinese M. J.* 49: 1146, 1935.

Insomnia in pregnancy is a very common condition. When it reduces a woman's sleep to one to two hours every night for a period of six to seven months, it becomes a rarity.

The common causes of insomnia, such as faulty habits of hygiene, acute and chronic disorders, were not present in this particular case. As to the cause of her insomnia, it was the author's impression that it was of psychic origin. The patient was not suffering physically from insomnia as indicated by the steady gain in weight and the satisfactory growth of the fetus. She came through the pregnancy and labor in good condition.

C. O. MALAND.

Raimann, E.: Therapeutic Interruption of Pregnancy in Nervous and Mental Diseases, *Wien. klin. Wchnschr.* 50: 166, 1937.

Because of the legal difficulties involved, and because there is no single disease for which interruption of pregnancy may be recommended without reserve, the disease and the patient as well as the social status and economic circumstances must all be taken into account. Of the diseases considered, viz.: Basedow's disease, status epilepticus, tabes, multiple sclerosis, and the psychoses schizophrenia, melancholia, and such a neurologic lesion as inoperable brain tumor, other factors such as duration of pregnancy and the ultimate effect on mother and child must also be considered. The psychiatrist and the gynecologist must work together. In many cases under combined management the patient may carry her pregnancy to term with appropriate mental treatment. All cases are treated on their relative merits and the dangers in each case should be carefully evaluated.

W. B. SERBIN.

Silva, Camillo: Acute Appendicitis Complicating Pregnancy and the Puerperium, *Ann. di ostet. e. ginec.* 15: 1475, 1936.

The author reports 27 cases of acute appendicitis during pregnancy and the puerperium and emphasizes the high mortality and difficulty of differential diagnosis. He states that pregnancy was interrupted in 36 per cent of the cases and the fetal mortality was 24 per cent.

The author claims that the therapy in acute appendicitis during pregnancy is exclusively surgical and occasionally cesarean section is necessary.

A. DARO.

Norton, James F., and Connell, John N.: Appendicitis Complicating Pregnancy and Labor, *Am. J. Surg.* 32: 325, 1936.

Acute appendicitis with peritonitis complicating labor, should be managed surgically as it is at any other time, and the labor allowed to continue with delivery through the birth canal, in the absence of an indication requiring a different obstetric procedure.

J. THORNWELL WITHERSPOON.

Stähler, Fritz: B₁-Hypovitaminosis in Pregnancy, München. med. Wchnschr. 84: 327, 1937.

Stähler reviews 15 patients of polyneuritis in pregnancy in whom he used vitamin B₁ (Betaxin) with marked success, giving 4 to 5 injections of 2 c.c. each every two to four days. He adds that it is also important to use a cod liver oil preparation with the vitamin B₁ treatment as the results appear to be quicker and more lasting.

C. E. PROSHEK.

Theobald, G. W.: Neuritis in Pregnancy Successfully Treated With Vitamin B₁, Lancet 1: 834, 1936.

Five pregnant patients with symptoms or evidence of neuritis were successfully treated with vitamin B₁ concentrate. Brief report is made of each case. Although not all of the findings in patients dying from vitamin B₁ deficiency can be explained directly by its absence, these changes may result from general disturbance in metabolism produced by this single deficiency.

The author feels that there is partial evidence supporting his dietetic deficiency hypothesis of the toxemias of pregnancy. He suggests the name "atelositetic neuritis of pregnancy."

Four of these five patients had all symptoms relieved by this diet.

H. CLOSE HESSELTINE.

Ferrigno, P.: A Case of Purulent Meningitis During Pregnancy, Clinica ostet. 15: 650, 1936.

The author presents a case of purulent meningitis caused by the meningococcus of Weichselbaum. Although the patient was a full term pregnant woman suffering with a chronic purulent otitis media, she recovered without surgical intervention upon the ear.

AUGUST F. DARO.

Harris, J. S.: Mental Disorder Associated With Child-Bearing, Brit. M. J. 1: 835, 1936.

Though it has long been recognized that no special form of mental disorder is associated with childbearing, various forms of mental disorder are encountered.

The author presents a discussion of three main groups as seen in 45 cases of mental disease associated with pregnancy. The manic depressive group consisted of two cases, a primipara and a multipara. Recovery ensued in from three to four months. The onset in both was postpartum and sudden. A delirious (acute confusional) group comprised 8 patients, of whom 6 recovered. A toxic focus was definite in one case. This group shows two types, a toxic and nontoxic. The onset may be sudden or gradual in the postpartum period. The schizophrenic group comprised 14 patients of whom 7 recovered. Time of onset of the derangement in 5 cases was during pregnancy, from the fourth to the eighth month. In a few the condition followed abortion, and in the remainder it occurred in the postpartum period, anywhere from one week to eight months after delivery. Periods of disability and recovery are discussed.

The mode of onset was definitely sudden in 15 cases, of whom 12 recovered, and gradual in 20 of whom 15 recovered.

The average duration of the psychosis was ten months in the 26 recoveries. The depressive types took a longer time to recover.

The patient delivered at the eighth month without difficulty. On the seventh postpartum day an abdominal cystotomy was performed when the foreign body, the slippery elm, was removed from the urethra and bladder. The patient had a satisfactory convalescence but a subsequent intravenous pyelogram showed marked pyelectasis of both kidneys and a small bladder having a grossly irregular outline.

H. CLOSE HESSELTINE.

Turner, G. Grey: Labour Complicated by Thrombosis of the Mesentery, *Lancet* 1: 802, 1937.

Ordinarily abdominal emergency operations are rare during pregnancy and are usually limited to those for the treatment of appendicitis, gallstones and torsion of pedunculated tumor. The author reports a case of resection of a portion of the small intestine done for a mesenteric thrombosis. The patient had previously had a perforating gastric ulcer repaired. A few years later during labor the patient presented evidence of intraabdominal hemorrhage. The uterus was emptied by cesarean section, after which the injured bowel was resected. Convalescence was stormy for several days. The patient had a miscarriage about one year later but no other pregnancies. No other complications developed during the next twenty-four years.

H. CLOSE HESSELTINE.

Yule, E.: Spontaneous Rupture of a Pregnant Uterus and Subsequent Atrophy of Fibroids, *Brit. M. J.* 1: 582, 1936.

The author had the rare opportunity to observe the presence of multiple fibromyomas during laparotomy for rupture of a pregnant uterus, and to confirm their subsequent atrophy at an operation for appendectomy a year later. Clinical notes on the case and the findings at operation are given. The treatment was cesarean section and repair of the rent in the uterus. The atrophy of the fibroids apparently occurred in the absence of any appreciable symptoms of an approaching menopause.

F. L. ADAIR AND S. A. PEARL.

Didier, Robert: The Enucleation of Large Fibroid Tumors During Pregnancy, *Gynéc. et obst.* 34: 363, 1936.

Altho many uterine fibroids permit the uninterrupted progression of pregnancy, certain of these tumors by virtue of their size or location will necessarily interfere with pregnancy at some stage.

Five cases are reported in which large uterine fibroids complicating gestation were removed by enucleation with no detrimental effect upon the pregnancy and with subsequent delivery of living babies. Four were at term, one at seven months. The smallest tumor weighed 600 gm., and the heaviest 3000 gm.

The author advises operation between the third and fifth month when the uterine wall is thick and enucleation is easily performed. Earlier, there is risk of abortion; later, the operation is more difficult. The uterine cavity must not be opened.

ARNOLD GOLDBERGER.

Siegmund, H.: Myoma Operations During Pregnancy With the Aid of Corpus Luteum Hormone Therapy, *Wien. klin. Wchnschr.* 49: 1193, 1936.

Myomas may easily but not always disturb the course of pregnancy. The effect is determined by the type of fibroid and its location in the uterus. Depending upon

Reeb and Irrmann-Wehrung: Appendicitis and Pregnancy, *Bull. Soc. d'obst. et de gynéc.* 25: 332, 1936.

Among 17,265 confinement cases, appendicitis occurred 22 times, an incidence of 1.27 per cent. According to the authors pregnancy does not predispose to appendicitis but it does favor recurrence of attacks, especially during the first few months. Acute appendicitis results in a certain percentage of abortions, deaths of infants and premature labors. Because pregnancy has a tendency to produce recurrences of appendicitis the authors advise the prophylactic removal of the appendix before marriage in all young women who have had a definite attack. If operation is necessary before the fifth month of pregnancy, a McBurney incision may be made. During the last four months a median incision is preferable. If the appendix can easily be removed, the pregnancy should not be disturbed but antispasmodics given after operation. If, however, the appendix is inaccessible, if there are adhesions, perforation, or gangrene with a localized peritoneal reaction, a cesarean section should first be performed and then the appendectomy. If drainage is necessary an extra incision should be made for this. If there is generalized peritonitis it is preferable to perform a subtotal hysterectomy after a cesarean section and then remove the appendix. Vaginal drainage should then be instituted. In all cases of peritonitis antigangrenous and anticolitis serotherapy should be administered both in the abdominal cavity and by intramuscular injections after operation.

J. P. GREENHILL.

Burnett, E. C., and McMenemey, W. H.: Rupture of the Normal Spleen in Pregnancy, *Brit. M. J.* 1: 1122, 1935.

Rupture of the spleen is a rare complication of pregnancy. There were only 15 cases reported in the literature up to 1930. In some the spleen is abnormal and direct trauma is a major factor.

In the present case the organ was normal and the trauma slight. The patient, aged forty-three, gravida xvi, was in the thirty-eighth week of pregnancy. She was healthy and had had no complications with previous labors. All 15 children were alive and well. She leaned back in bed to switch out the light above and behind her. On reaching out with her left hand, she was seized with a pain under the left costal margin and was unable to resume her original position for some time. The pain persisted all night. She vomited once. At 6 A.M. her temperature was 99°, pulse 80. There was pain and tenderness in left costal margin. Pulse rose gradually to 132, and she grew weak. The pain persisted vaguely in both flanks. Her abdomen was tense, heart and lungs negative. The fundus was at the xiphisternum and the uterine wall was felt contracting regularly. She was not in labor.

The fetus was in O.L.A., head not yet engaged. The fetal heart was not heard, and the patient said she had felt no movements since onset of pain. There was diffuse tenderness in both flanks and dullness in left flank, but no pain in left shoulder. The external os was closed. Immediate laparotomy revealed free blood in the abdominal cavity coming from a ruptured spleen. Splenectomy was done after cesarean section due to advanced stage of pregnancy. Except for congestion no pathologic feature was present in the spleen.

F. L. ADAIR AND S. A. PEARL.

Farncombe, R.: Foreign Body in the Bladder Associated With Pregnancy, *Lancet* 2: 825, 1935.

The patient had attempted to induce an abortion by using slippery elm in the third month of pregnancy. It was inserted and she thought absorbed. Because of urinary incontinence and dysuria an examination was made at the seventh month when a mass was found in the base of the bladder.

Items

American Association of Obstetricians, Gynecologists and Abdominal Surgeons

Rules governing the award of "The Foundation Prize" of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons.

1. "The award which shall be known as 'The Foundation Prize' shall consist of \$500.00.

2. "Eligible contestants shall include only (a) internes, residents, or graduate students in Obstetrics, Gynecology or Abdominal Surgery, and (b) physicians (with an M.D. degree) who are actively practicing or teaching Obstetrics, Gynecology or Abdominal Surgery.

3. "Manuscripts must be presented under a nom-de-plume, which shall in no way indicate the author's identity, to the Secretary of the Association together with a sealed envelope bearing the nom-de-plume and containing a card showing the name and address of the contestant.

4. "Manuscripts must be limited to 5,000 words, and must be type-written in double-spacing on one side of the sheet. Ample margins should be provided. Illustrations should be limited to such as are required for a clear exposition of the thesis.

5. "The successful thesis shall become the property of the Association, but this provision shall in no way interfere with publication of the communication in the Journal of the Author's choice. Unsuccessful contributions will be returned promptly to their authors.

6. "All manuscripts entered in a given year must be in the hands of the Secretary before June 1.

7. "The award will be made at the Annual Meeting of the Association, at which time the successful contestant must appear in person to present his contribution as a part of the regular scientific program, in conformity with the rules of the Association. The successful contestant must meet all expenses incident to this presentation.

8. "The President of the Association shall annually appoint a Committee on Award, which, under its own regulations shall determine the successful contestant and shall inform the Secretary of his name and address at least two weeks before the annual meeting."

JAS. R. BLOSS, M.D., *Secretary*.
418 Eleventh Street,
Huntington, W. Va.

the location of the fibroid and its effect on the pregnancy, the latter may either be conservatively carried to term with little or no treatment or operative treatment may become necessary. This may consist of a myomectomy preserving the pregnancy while in some cases the entire uterus must be removed. The author reports two cases treated by conservative myomectomies and then pregnancies being fortified with corpus luteum hormone. Both patients were at term delivered of living healthy babies.

W. B. SERBIN.

DaLéas, P.: Malaria and Pregnancy, *Rev. franç. de gynéc. et d'obst.* 31: 232, 1936.

The author has had an extensive experience in Indo-China treating pregnant women who had malaria. His experience is based upon 8,000 deliveries. He found that malaria affects pregnancy just as any other acute and chronic infectious disease. Because malaria affects the liver and kidneys, complications of these organs frequently arise. On the other hand, pregnancy occurring in a woman once infected with malaria may suddenly produce a lighting up of the old infection. Frequently the child is infected in utero. This often results in interruption of pregnancy. The children who are born only slightly infected have a good prognosis.

J. P. GREENHILL.

Ghose, Sudhangsu Kumar: Malaria as a Complication in Pregnancy, *Calcutta M. J.* 30: 541, 1936.

The author reports a case of malaria complicating an eight-month pregnancy and terminating in the death of mother and fetus. The clinical course closely simulated acute yellow atrophy of the liver. The salient points to be learned from this fatality are as follows: (1) that the presence of intense vomiting and jaundice led to a diagnosis of toxemia rather than malaria; (2) the importance of blood examination in fever cases. This life could have been saved by an earlier detection of the malaria parasite in the blood and antimalarial therapy. (3) In spite of a heavy infection of the maternal blood, no malaria parasites could be found in the cord blood or in the heart of the dead fetus.

F. L. ADAIR AND S. A. PEARL.

Morra, Giuseppe: Nicotine Intoxication and Pregnancy, *Ginecologia (Torino)* 9: 996, 1935.

After reviewing the literature, the author discusses the pharmacology and toxicology of nicotine.

From his personal research on the chronic experimental nicotine intoxication during gestation he forms the following conclusions: (1) Nicotine experimentally introduced into the maternal organism can pass through the placental barrier, and can be detected in the fetal tissue by biologic methods. (2) The course of pregnancy is influenced relatively little in the rabbits subjected to chronic nicotine poisoning. Moreover, prematurity of birth was observed in the poisoned animals.

AUGUST F. DARO.

Books Received

APPROVED LABORATORY TECHNIC. By John A. Kolmer, Professor of Medicine, Temple University, etc., and Fred Boerner, Assistant Professor of Bacteriology, School of Medicine and Graduate School of Medicine, University of Pennsylvania, etc. Second edition. Rewritten, revised and reset, with 12 plates and 380 illustrations in the text, 893 pages. D. Appleton-Century Co., New York, 1938.

FEVER THERAPY. Abstracts and discussions of papers presented at the First International Conference on Fever Therapy, March 29-31, 1937. College of Physicians and Surgeons, Columbia University, New York. 486 pages. Paul B. Hoeber, Inc., New York, 1938.

MILESTONES IN MEDICINE. Laity lectures of the New York Academy of Medicine. Introduction by James Alexander Miller, M.D. 276 pages. D. Appleton-Century Co., New York, 1938.

DIE VITAMINE IN DER CHIRURGIE. Von Professor Dr. Erich Schneider, Chirurgische Univ. Klinik, Freiburg i.B. Verlag von Ferdinand Enke, Stuttgart, 1938.

EIGHTH INTERNATIONAL CONGRESS OF MILITARY MEDICINE. Brussels, 1935. Report of Captain William Seaman Bainbridge. U. S. Gov. Printing Press, Washington, 1937.

DISEASES OF WOMEN, for the General Practitioner. By Paul Titus, M.D., Obstetrician and Gynecologist to the St. Margaret Memorial Hospital, Pittsburgh, etc. Edited by Morris Fishbein, M.D. Illustrated, 320 pages. National Medical Book Co., Inc., New York, 1937.

OPERATIVE GYNECOLOGY. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology and Obstetrics, and Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Fifth edition, entirely revised and reset. With 1,264 illustrations including three color plates on 1,076 pages. The C. V. Mosby Company, St. Louis, 1938.

A HISTORY OF WOMEN IN MEDICINE. From the earliest times to the beginning of the nineteenth century. By Kate Campbell Hurd-Mead, M.D. Illustrated, 569 pages. The Haddam Press, Haddam, Conn., 1938.

THE PHYSICIAN'S BUSINESS. Practical and Economic Aspects of Medicine. By George D. Wolf, M.D., Attending Oto-Laryngologist, Sydenham Hospital, New York City, etc. Foreword by Harold Rypins, M.D., F.A.C.P. With 57 illustrations, 384 pages. J. B. Lippincott Company, New York, 1938.

American Board of Obstetrics and Gynecology

The general oral, clinical and pathological examinations for all candidates (Groups A and B) will be conducted by the entire Board, meeting in San Francisco, California, on June 13 and 14, 1938, immediately prior to the meeting of the American Medical Association.

Application for admission to the June, 1938, Group A examinations must be on an official application form and filed in the Secretary's Office before April 1, 1938.

The annual informal Dinner and General Meeting of the Board will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, will be the guest speaker, and the Diplomates certified at the preceding days' examinations will be introduced individually. All Diplomates are invited to attend the dinner meeting, and to bring as guests their wives and any persons interested in the work of the Board.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

International Congress for Obstetrics and Gynecology

The International Congress for Obstetrics and Gynecology will convene at Amsterdam, Holland, from May 4 to 8, 1938. The program of the proceedings was published in the January issue of this JOURNAL. For further information about travel arrangements, hotel reservations, etc., apply to Messrs. Thos. Cook & Son, 587 Fifth Avenue, New York City.

Erratum

In a paper entitled "A Combined Operation for Complete Hysterectomy," by S. H. Geist, published in the June, 1937, issue of this JOURNAL (p. 1081), I inadvertently omitted a reference to the effect that a similar procedure was described in Döderlein and Kroenig's *Operative Gynecology* (Fifth Edition, Thieme, Leipzig, 1924, p. 554). A combined operation was referred to in which, after liberating the cervix, the uterus was removed from above. The method was discontinued, however, with the advent of the Trendelenburg posture.

S. H. GEIST.

largely acute and transient. I believe that such conditions are seldom, if ever, the causative factor in recurrent abortions.

In considering defective germ plasm, Streeter says, "It must be understood that defective germ plasm is described on the basis of behavior rather than microscopic appearance. **** If the building materials are good, then the egg is good. In such cases endocrine influences should not be powerful enough to disturb normal development." Regarding the last sentence, the work of many investigators proves that such is not the case in experimental animals, and it seems unreasonable to believe that the human being is an exception. The many reported successes of treatment on endocrine bases in such cases seem to indicate that endocrine factors *are* powerful enough to disturb normal development of the human fertilized egg.

Mall states that of human abortion ova dating from the first month, he found only a fifth normal. There is no reason to disbelieve that defects do occur in the germ cells which are inherent in them, and which give rise to faulty products of conception which of themselves die and are aborted. There may be other abnormalities of the germ cells and later the embryo, of chemicobiologic nature, which are not demonstrable microscopically, but which may be sufficient to prevent continued development. In such cases, endocrine factors probably play a paramount rôle.

In the female there is a structure which mirrors accurately the hormone factors which are responsible for its cyclic histologic appearance, viz., the endometrium. Especially can the story of these factors be read in the immediate premenstrual endometrium. Varying types and degrees of sex hormone imbalance in the female are reflected in varying types and degrees of departure from normal of this structure. The hormones which are responsible for the type of endometrium present are elaborated by the same organ, and more particularly the same structure in it, viz., the follicle and resultant corpus luteum, which produces the ovum. These in turn are dependent upon certain sex hormones of the anterior hypophysis.

Normal conception and pregnancy are dependent upon the union of two normal germ cells, and a normal soil for the development of the fertilized ovum, i.e., a normal endometrium. It is possible to discern microscopically from the examination of the premenstrual endometrium even minor grades of departure of this structure from normal. Since such abnormalities found here represent sex hormone deficiencies or imbalances in the individual, it seems reasonable to suppose that disorders of fertility in these cases may be due either to the fact that such hormonal imbalance simultaneously produces abnormal ova, or, the fertilized ovum being so intimately dependent upon this endometrial soil for its development, that these defects in the endometrium *may* be

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Original Communications

SEX HORMONE FACTORS IN RECURRENT ABORTION AND STERILITY

LYMAN W. MASON, M.D., DENVER, COLO.

THE causes which have been ascribed for spontaneous abortion are legion. While it is possible that all of these causes have applied to individual cases, none of them has been fundamental. Especially is this true in so-called habitual abortion, a better term for which is recurrent abortion. The purpose of this paper is to call attention to certain demonstrable pathologic factors which link sterility or diminished fertility in some cases, and recurrent abortions, as parts of the same fundamental abnormality, and to present a small series of cases which have been successfully treated on this basis. Those cases of sterility in the female which are due to more or less gross anatomic defects, such as tubal closure, for example, are not within the scope of this discussion. Cases of diminished male fertility, of the type to which Moench and I have called attention, probably fall within it.

When the cases mentioned above are excluded, those of sterility or diminished fertility which remain, and spontaneous abortions, particularly those of the recurrent type, must be due to abnormalities of the seed or the soil, or both, i.e., the ovum, the spermatozoon and/or the endometrium. It is my opinion that the endometrium, except in the rare case, but reflects the endocrine factors which produce the histologic changes in it. The endometrium is singularly resistant to inflammatory or infectious processes, and those which may at times inflict it are

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

sible for the development and maturity of the Graafian follicle, and probably both, but particularly the latter, for the development of the corpus luteum.

A normal premenstrual endometrium, therefore, presupposes a normal ovarian cycle, with a normal elaboration of, and balance between, estrin and progesterone. This in turn presupposes a normal activity of the

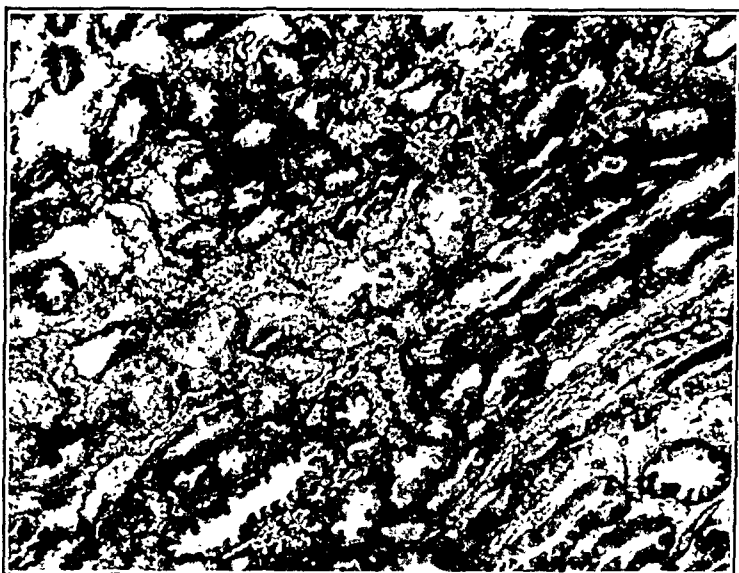


Fig. 1.—Normal endometrium.

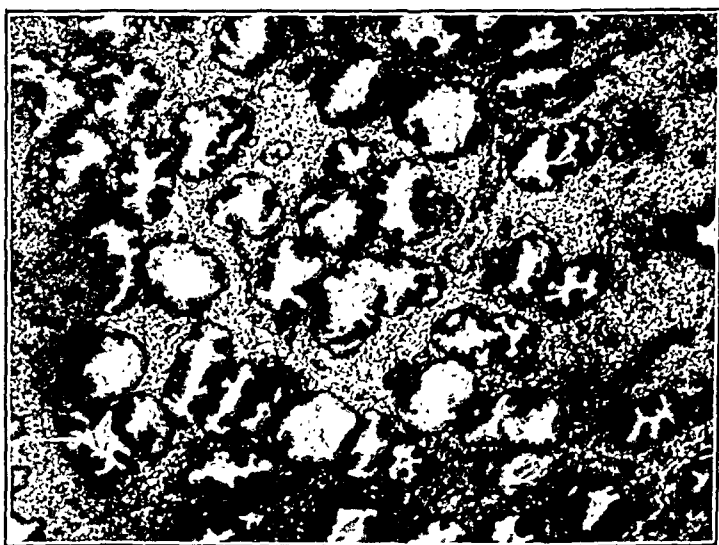


Fig. 2.—Normal endometrium.

sex hormones of the anterior hypophysis. Since studies have increasingly shown the close interrelationship between all the endocrine glands, and the effects produced upon the rest by abnormalities in one, it follows that the presence of such a normal endometrium is probably evidence of a normal balance between all the endocrine glands, at least so far as the female sex cycle is concerned.

responsible for the defects which may or may not be microscopically demonstrable in the aborted embryo or fetus. Also both factors may be operative together. The same may be true for the entire failure of conception in some of the cases.

In the male, there is no structure such as the endometrium in the female which so well reflects sex hormone states. However, evidence seems to indicate that an abnormally high percentage of grossly abnormal sperms in a semen specimen is an index of lowered fertility in that individual, resulting in failure of impregnation or an increased incidence of abortions. I have previously stated that it is my opinion that factors inherent in the male germ cells themselves are responsible for the abnormal specimen as a whole. In other words, the endocrine factors which are responsible for the abnormally high percentage of grossly abnormal forms also operate to diminish the fertility of those sperms which do appear normal microscopically. Otherwise it is difficult to understand why, even in such specimens, fertility is diminished, when the apparently normal sperms outnumber the grossly abnormal ones many thousands to one.

It is in order to review briefly the hormone factors responsible for the endometrial changes which take place during the menstrual cycle. Immediately following menstruation, the endometrium has been desquamated until only the basal layer remains on the uterine musculature. The glands are straight, widely spaced and compact, being lined by a single layer of low columnar or cuboidal cells with central nuclei. By this time, a primordial follicle in the ovary has begun to develop. During the period of its development estrin is elaborated, under whose influence a hyperplasia of the endometrium occurs, marked by an increase in thickness, an increased vascularity, and by a hypertrophy and hyperplasia of the uterine glands. Somewhere about midinterval the follicle ruptures, the ovum is extruded, and the ruptured follicle is converted into the corpus luteum. The elaboration of estrin is continued by this body, but the characteristic hormone of the corpus luteum is progesterone. The hyperplasia of the glands therefore continues, but under the action of progesterone certain premenstrual changes occur in the hyperplastic glands. These take on a definite secretory appearance, marked microscopically by columnar epithelium with basal nuclei, vacuolization of the cells, distention of the lumina by secretion, and a distinct "fuzziness" of the inner gland borders. Figs. 1 and 2 show well these normal premenstrual characteristics.

The development of the Graafian follicle and subsequent corpus luteum is dependent upon the sex hormone or hormones of the anterior hypophysis. While not yet proved, the mechanism is somewhat easier to understand if we follow the postulation of two such hormones, the follicle stimulating hormone and the luteinizing hormone. The first is respon-

gradual in its effect, and cumulative, in the decidua and/or in the embryo and its nutritive processes, i.e., the trophoblast or developing placenta.

The same reasoning applies to those cases in which conception does not occur, and in which examination of the premenstrual endometrium shows evidence of progesterone deficiency. Both of these conditions may therefore be considered parts of the same fundamental condition, viz., a deficient corpus luteum function by which insufficient progesterone is elaborated. In lesser degree it may permit the nidation of a fertilized ovum but be unable to meet the demands of continued development. In greater degree the endometrium is so poorly prepared that nidation itself is impossible. As stated previously, the assumption that the endocrine factors responsible for this condition may already have produced an ovum (or analogous factors in the male the spermatozoa) potentially below par seems not unreasonable.

In the cases described below, each premenstrual endometrium, except one, which it was possible to obtain, shows evidence of corpus luteum (progesterone) deficiency. From the results of therapy in those cases in which an endometrium specimen was not obtained, the conclusion that such a deficiency was present seems justified.

In the past, commercial preparations of progesterone of proved potency have not been available, and in the treatment of these cases pregnancy urine extracts have been used. While observation has not shown such results in the human ovary as occurs in the ovaries of experimental animals following injection of pregnancy urine extracts, it is possible that an action considerably short of this might stimulate the corpus luteum to adequate activity.

Mazer and Goldstein call attention to the fact that even in cases of recurrent abortion, the anterior pituitary-like hormone is always present in large amount in the urine and for this reason do not believe that such therapy is indicated in these cases. I infer from their text that their reference is to the hormone as obtained from the pituitary itself. They also point out that pituitary implants and injections of pituitary extracts produce superovulation and seem to cause or favor abortion instead of preventing it. This is in line with the observations of the D'Amours and others that extracts obtained from the pituitary are predominantly follicle stimulating, while those obtained from pregnancy urine and placenta are predominantly luteinizing. While the urine of an individual case might contain sufficient luteinizing hormone to give a characteristic reaction in the ovaries of the mouse or rat, it might still be insufficient for that individual's pregnancy, which insufficiency could be supplied by the luteinizing hormone present in greater amounts from

In another paper, photomicrographs of premenstrual endometriums are shown which grade almost imperceptibly from the normals described above and illustrated, to the typical "Swiss cheese" pattern, which is the one most familiar to the pathologist. Curettages are not usually done for the clinical conditions which accompany or result from those endometriums of considerably less pathology, which are here under discussion. However, it is these types which are of importance from the standpoint of recurrent abortions and other disturbances of fertility.

It is of much interest that these departures from normal all seem to begin with evidences of diminishing progesterone influence on the uterine glands, as marked by their lessened secretory appearance immediately before menstruation. In other words, the corpus luteum seems to be at fault. In a succession of endometriums of increasing pathology, signs of corpus luteum activity diminish until there is no evidence of it at all, in which case we infer that ovulation has not occurred. In these marked cases, all menstrual rhythm is frequently lost, bleeding is continuous, and the endometrium assumes the "Swiss cheese" appearance, associated with polycystic ovaries, in which there is no evidence of current corpus luteum activity.

It is known that the corpus luteum is necessary for the continuance of early pregnancy, possibly through the second month or a little longer, but that its removal after a certain time in the human is not necessarily followed by abortion. Evidence has accumulated to show that the placenta also has an endocrine function similar to, and possibly identical with, the corpus luteum, since the same hormones are obtainable from it. As the pregnancy progresses, and beginning with the development of the placenta, the activity of the corpus luteum wanes, and its function in the continuation of the pregnancy is evidently taken over by the placenta.

It is significant that in cases of recurrent abortion, most of them occur between the second and third month. This is also true of the occasional abortion. It is at about this time that the corpus luteum ceases to be necessary for the continuation of the pregnancy, its hormone function being assumed in full probably by the placenta, as noted above. Is it not possible that abortions at this time are due to the fact that the corpus luteum activity ceases too soon, or that the ascension of the placental elaboration of hormone is too slow, so that there is a period of time when progesterone sinks below a level necessary for the continued development of the embryo, and abortion results? This may be due fundamentally to an insufficiently fertile decidua, or to direct injury to the embryo, or both. In those cases where examination of the premenstrual endometrium shows already evidence of corpus luteum deficiency, the damage resulting in abortion at this usual time may be

further pregnancies to the present time (March, 1937). Evidence in this case points to a hormone abnormality which is gradually increasing in severity.

CASE 2.—D. B., aged nineteen years, first seen Oct. 24, 1932, had been married for two and one-half years. First pregnancy occurred within ten months after marriage. There was a spontaneous abortion of this pregnancy at two and one-half months. She was referred for consultation because another pregnancy had not occurred. Complete sterility study was done and both husband and wife were considered normal. However, conception did not occur again until following the menstrual period of Sept. 28, 1934. No treatment was given, and abortion occurred Nov. 21, 1934. After bleeding and cramping had started, morphine, bed rest, and pregnancy urine extract were used without effect upon the course of the abortion. After this abortion, the case was restudied, including the premenstrual endometrium. Again it was considered normal (Fig. 4). It is the only premenstrual endometrium yet examined in a patient who has had as many as two successive spontaneous abortions, which has been considered normal.



Fig. 4.—Case 2.

The next probable pregnancy dated from the menstrual period of June 15, 1936. She was examined July 30, and diagnosis of probable pregnancy made. She presumably aborted August 10, while away on a vacation.

The next pregnancy dates from the menstrual period of Oct. 5, 1936. Treatment consisting of 2 c.c. of pregnancy urine extract was begun within two weeks after the missed menstrual period, and was given twice weekly until Feb. 2, 1937, since which time it has been used once a week. The pregnancy has been uneventful except for severe intermittent uterine cramps which began suddenly on Dec. 9, 1936, and which stopped entirely, not to recur, within an hour after the injection of an additional 2 c.c. of the extract.*

CASE 3.—F. M., aged thirty-two years, was first seen in 1933 because of severe menorrhagia. This patient's premenstrual endometrium is shown in Fig. 5. It is obviously deficient in progesterone influence. Physical examination was negative

*This patient was treated as outlined in the text until one month before term, and was delivered at term, July 14, 1937, of a normal child.

the urines of other pregnancies. While most abortions, particularly of the recurrent type, occur early, abortion at any time during a pregnancy may occur from an imbalance of estrin and progesterone, which may not have been present from the beginning of the pregnancy or before.

The following cases are presented:

CASE 1.—I. M., aged twenty-six years, first seen Dec. 19, 1929. First pregnancy occurred shortly after marriage in 1926 and was normal throughout. Last menstrual period was Oct. 23, 1929. Spontaneous abortion occurred Dec. 25, 1929. Next pregnancy dated from menstrual period of Dec. 29, 1930. In spite of the usual treatment of sedation and bed rest, abortion occurred March 11, 1931. After this abortion, complete sterility study was made. All results were negative except for evidence in the premenstrual endometrium of progesterone deficiency (Fig. 3). Basal metabolism rate was plus 4 per cent.



Fig. 3.—Case 1.

While the glands in this specimen are hyperplastic, and show considerable infolding, both glands and stroma are rather compact, and are lacking in that "succulent" appearance of the normal premenstrual endometrium. The glands are definitely deficient in secretory appearance.

The next pregnancy dated from the menstrual period of Aug. 23, 1932. On October 27, slight bleeding occurred; no cramps. All other abortions had begun in this manner. On this date, 2 c.c. of pregnancy urine extract were given, and bleeding stopped within six hours. This amount was repeated on alternate days for two weeks, when it was discontinued. On December 6, there was again slight bleeding, which stopped within three hours after the injection of 2 c.c. of the extract. After this, 2 c.c. of the extract were given weekly until March 1, 1933, when the injections were discontinued. She was delivered in April, about one month prematurely, of an otherwise normal baby girl which lived and developed normally.

The next pregnancy dated from the menstrual period of Sept. 18, 1934. Thinking that perhaps the glandular system had been improved by the former pregnancy, no treatment was given during this pregnancy. The membranes, probably defective, ruptured at five and one-half months, followed by abortion. There have been no

Sterility study was made in this case, which was negative, except for the abnormal premenstrual endometrium, which is sufficient to explain both the scanty menstruation and the sterility. Not only is the progesterone activity markedly deficient, but the endometrium is generally hypoplastic (Fig. 6).

For various reasons, this patient was not treated, and the case is included because of the type of endometrium found.

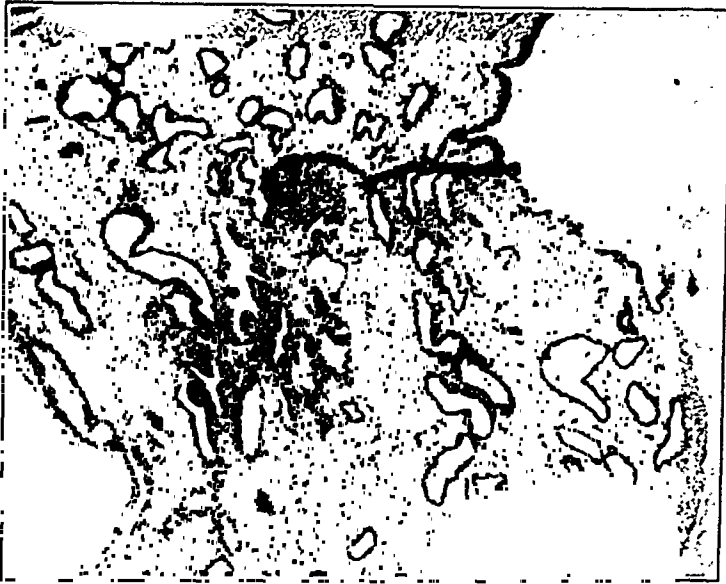


Fig. 6.—Case 5.



Fig. 7.—Case 6.

CASE 6.—M. R., aged thirty years. Her first pregnancy occurred in 1931, two years after marriage, following rather promptly the discontinuance of contraceptives. This pregnancy was complicated by an attack of pyelitis, but continued to term. Delivery was without incident.

Contraceptives were resumed following this pregnancy, and were used until June, 1935. The next pregnancy dated from the menstrual period of November,

except for marked endocarditis. Administration of pregnancy urine extracts was always effective in controlling the excessive menstrual bleeding, frequently stopping it within three or four hours.

She had two children, six and two years of age. She stated that she flowed regularly at what would have been menstrual periods for three months during the first pregnancy, and for five months during the second. The first baby was born one month prematurely, the second at term.

Her last pregnancy dated from the menstrual period of May 15, 1935. There was a scanty flow in June and July. While recognizing the hormone imbalance in this case, no treatment was given, as the heart condition made an interruption of the pregnancy not inadvisable. She did abort spontaneously Aug. 1, 1935, at about two and one-half months.

CASE 4.—V. W., aged twenty-seven years, was first seen March 2, 1936. This woman had been married for two and one-half years. There had been spontaneous abortions in June, 1934, and in July, 1935, both between the second and third months.



Fig. 5.—Case 3.

Last pregnancy dated from the menstrual period of Jan. 22, 1936. The case was studied as well as could be, since she was already pregnant when first seen. All results were negative except a basal metabolism rate of minus 11 per cent. She was placed on $\frac{1}{4}$ gr. of thyroid twice daily, which was subsequently increased to $\frac{1}{2}$ gr. Pregnancy urine extract, 2 c.c. twice a week, was given until after the fourth missed menstrual period, when it was reduced to once a week, and it was continued in this dosage until the patient went spontaneously into labor.

It is interesting that this patient delivered about three weeks past term. The baby showed evidence of intrauterine loss of weight, marked chiefly by flabbiness and laxness of the abdomen, and the placenta was markedly fibrous and calcified. The entire pregnancy was normal and uneventful, and the subsequent development of the baby was normal.

CASE 5.—B. W., aged thirty-one years, was first seen in 1932. This patient had been married for five years. No contraceptives had ever been used, but conception had not occurred. Menstrual history was essentially negative, except that there was occasional dysmenorrhea, and flow tended to be scanty.

Patient next seen in September, 1935, at which time she was complaining of dysmenorrhea, which she had not had previous to her marriage. This was relieved by dilatation of the cervix. Pelvic examination was entirely negative except for the absence of the right ovary.

Next seen in July, 1936, because pregnancy had not occurred since discontinuance of contraceptives in October, 1935. Complete sterility study was made, with negative results, except for the appearance of the premenstrual endometrium (Fig. 8). Here also the appearance of the glands denotes a deficient corpus luteum activity. The resemblance of this specimen to that shown in Fig. 7 is rather marked.

No treatment was given at the time, but conception not having occurred by February, 1937, treatment as outlined in the preceding case was instituted. She has menstruated once since it was begun.

This case is included before the results of treatment are known for the purpose of illustrating the type of endometrium found.

An examination of the premenstrual endometrium forms an indispensable part of every investigation to determine the cause of failure of conception or of recurrent abortions. As has been stated elsewhere by myself and others, a curettage of sufficient thoroughness to secure ample tissue for microscopic examination is a simple office procedure, practically without risk, and devoid of the need for anesthesia. In no other way can these relatively minor hormone deficiencies be determined, without which rational therapy is impossible.

It is interesting that in one of the cases cited (I. M.) treatment with pregnancy urine extract was discontinued two months before term, and this pregnancy ended prematurely at eight months. In another (V. W.), it was continued until labor began spontaneously, and this patient went over term three weeks. The placenta had a marked "senile" appearance, and the baby, as stated, showed evidence of intrauterine loss of weight, presumably because of diminished nutrition through the fibrous and calcified placenta.

Many adverse reports have appeared in the literature regarding the treatment of threatened abortion with the anterior pituitary-like hormone. It should be repeated that it has been shown that such hormones obtained from the pituitary itself, are predominantly follicle stimulating, while those obtained from pregnancy urines, and probably those from placentae, are predominantly luteinizing. Both types of preparations, of course, contain both hormone fractions.

Another point to emphasize is, that if demonstrable hormone deficiency is present even before the pregnancy begins, this effect on the nidatory soil, and probably on the developing embryo and its nutritive processes, is probably continuous and cumulative to the time of the abortion. *It is evident, therefore, that a threatened abortion may represent, not the beginning of trouble, but the end of a damaging process which is past help.* If this view of the matter is taken, one does not wonder that treatment instituted at the time an abortion is threatened is so frequently fruitless.

Treatment along hormone lines, and any other indicated, as for example thyroid in cases of hypothyroidism, and at all times an adequate

1935, and spontaneous abortion occurred the latter part of December. (Both the pregnancy and abortion here are assumed, as neither was verified.)

Following this, complete sterility study was done. All results were negative except for the appearance of the premenstrual endometrium (Fig. 7). While the appearance of the glands is proof of a functioning corpus luteum, its influence on the glands is obviously subnormal.

Pregnancy had not occurred following this episode. Menstruation occurred Oct. 4, 1936. Pregnancy urine extract, 1 c.c., was given three times a week during the two weeks preceding the next expected period. It began October 30. The same procedure was followed during the two weeks preceding the next expected period in November. This did not occur, and pregnancy test was made three weeks later and found strongly positive. Pregnancy was subsequently diagnosed clinically.

The patient continued to receive 1 c.c. of the extract twice a week. During this time she was working from ten to sixteen hours daily in chemical research, in addition



Fig. 8.—Case 7.

to which during the Christmas holidays she was quite active socially. She contracted influenza on December 29, which was epidemic in Denver at the time, and was quite ill, with high temperature. She aborted Jan. 3, 1937. It does not seem that this pregnancy had a reasonable chance, although I feel that more frequent and larger doses of the extract might have prevented the abortion, since this one occurred at the usual time, viz., between the second and third month. This patient is the only failure to date, in the type of case under discussion, when treatment could be started as soon as the pregnancy was diagnosed.*

CASE 7.—B. S., aged twenty-seven years, was first seen in January, 1935, shortly after her marriage. At this time patient stated that her menstrual periods were normal. However, she also stated that seven years previously, the right ovary had been removed at the time of an appendectomy because it was "cystic."

*This patient is again pregnant, dating from Oct. 5, 1937. Again conception did not occur until after treatment during the last half of a menstrual cycle with pregnancy urine extract. Since the first missed menstrual period, she has received proluton in diminishing doses from 1 unit three times a week to 1 unit once a week. She is now five months pregnant. The present therapy will be continued to shortly before term. To date there has been no threatened interruption of the pregnancy.

of conscious efforts to control fertility. In the strictest sense, voluntary control of fertility is of sociologic rather than of medical concern, but so far as voluntary control affects the public health, it also becomes a medical problem. Both groups of factors may be present at the same time, but for convenience they will be discussed separately.

Present knowledge concerning the involuntary causes of variations in fertility relates to those factors which lessen fertility or produce sterility. They may be classified as (1) those which interfere with the possibility of the fertilization of an ovum, and (2) those which interfere with the wife's ability to bear a live child. It is, of course, well known that absolute sterility is a rare phenomenon. Meaker found that only 30 per cent of the patients coming to him for the medical treatment of sterility could be classified as absolutely sterile. Fertility is not an all-or-none proposition.

Reynolds and Macomber,⁵ in experiments with rats, found that the fertility of a mating was the product of the fertility of the individual partners; and Meaker,⁶ in discussing the problem of human fertility, expresses the situation as follows: "The human animal . . . is by comparison with others a poor breeder, rarely endowed with . . . absolute fertility. . . . Most couples who succeed in reproducing do so in spite of certain imperfections in the conceptive mechanism; . . . in other words, most people are relatively and not absolutely fertile."

The importance of any one cause of sterility or infertility is unknown. Sterility, which is the only aspect of the problem which has been studied to any extent, is seldom caused by a single factor. Usually there are several underlying causes, and conception does not take place until most or all of these difficulties have been eliminated. Most pathologic conditions are temporary and reversible with treatment. Thus, a couple may be infertile for a period and then become fertile, or vice versa. The incidence of involuntary sterility or infertility in broad population groups at any one time is unknown.

In a recent study by the Milbank Memorial Fund staff of the preclinic control of fertility by a group of women who subsequently attended a birth control clinic in New York City,^{7, 8} a small amount of information was available concerning the incidence of gross pathology in the group.*

*The Milbank Memorial Fund was requested by Mrs. Margaret Sanger to make a study of a group of patients of the Birth Control Clinical Research Bureau in New York City. The group selected for study comprised all the women who first came to the clinic from the Borough of the Bronx in 1931 and the first half of 1932 and were still living in the Bronx in 1933 and 1934, when the study was made. The records were obtained by the author in personal interviews with the women in their homes. Each record contains a complete fertility history which includes the dates of marriage and the date and type of termination of each pregnancy, as well as the history of associated pathology and information concerning contraceptive practices before each pregnancy. All data here published relate to the fertility of these women before attendance at a birth control clinic. The types of contraception practiced were those in general use in the population at large.

The following are examples of the cases excluded because of the history of pathology which probably interfered with fertility:

- (1) Unilateral oophorectomy (Case 823).
- (2) Marked retroversion; tubes inflated and cervix cauterized before conception took place (Case 990).
- (3) Pelvic abscess following self-induced abortion (Case 522).
- (4) Husband impotent because of severe endocrinopathy; conception followed endocrine therapy (Case 608).

calcium and vitamin intake, should be begun as soon as pregnancy is suspected, in all patients with any past history of reproductive difficulty. Also adequate preparations in these cases should probably be given more frequently and in larger doses than have heretofore been done.

There are good reasons for believing that progesterone itself might serve better in these cases than the attempt to stimulate the ovary or more particularly the corpus luteum to the elaboration of increased amounts of its own hormone by the use of pregnancy urine extracts. However, as is well known, no such preparations of progesterone of proved potency have been available in commercial quantities. It may be that they are now on the market, but if so, they have still to be proved clinically.

THE MEDICAL ASPECTS OF VARIATIONS IN FERTILITY*

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(From the Milbank Memorial Fund)

THE medical profession has long been concerned with individual problems of fertility and sterility, but the larger problems of broad variations in fertility in population groups have been studied mainly by sociologists and students of population problems. They have found that birth rates are low among the white-collar and professional classes and high among laborers, and that urban birth rates are considerably lower than rural birth rates.^{1, 2} The urban groups are not producing enough children to reproduce themselves and replacements for our future population are coming mainly from rural groups. Students of the problem are questioning whether migration into the cities is selecting the best of these stocks, leaving the groups with least cultural or genetic endowment as a future population reservoir. Recent researches^{3, 4} have shown that the differentials in the birth rate may be due to differences in the prevalence and effectiveness of contraception in the various social classes, rather than to inherent biologic differences in fertility. There may be, in addition, a differential prevalence of sterility, but we have no information concerning the prevalence of sterility in specified population groups. The problems of sterility and of voluntary control of fertility are of special interest to obstetricians and gynecologists, and for this reason the broader problems of variations in fertility become of immediate medical concern.

The causes of variations in fertility may be classified into two groups: (a) involuntary causes—those which are due to differences in physiologic activity or intercurrent pathology and which happen without reference to any effort on the part of individual couples to control their fertility, and (b) voluntary causes—those which are the direct result

*Adapted from a paper read before the joint meeting of the American Statistical Association and the Population Association of America, Chicago, Illinois, December 30, 1936.

The influence of pregnancy wastage on birth rates has been difficult to determine accurately. In the study previously cited and in two additional studies from the Milbank Memorial Fund, the fertility records included the date and type of termination of every pregnancy. The women showed little or no reticence in discussing past abortions when they knew the confidential nature of the individual records. Information concerning abortions appears, therefore, to be unusually reliable, and its reliability is confirmed by the consistency of the data under all types of analysis. It was found that the average incidence of accidental pregnancy wastage (stillbirth, spontaneous abortion, etc.) was between 10 and 12 per cent of all pregnancies, and was not significantly different in several economic groups or in three religious groups, nor did it change with increasing length of marriage or order of pregnancy. There was also no indication that its prevalence had changed within the periods

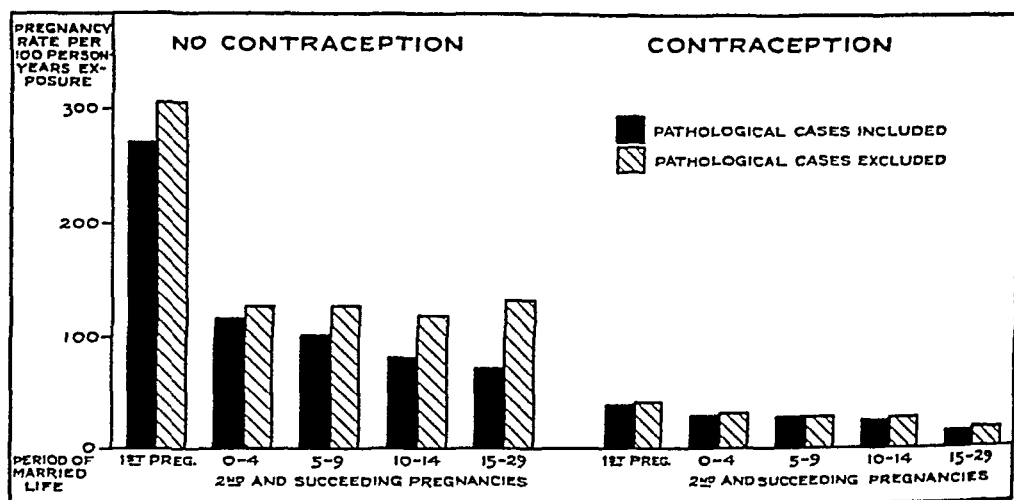


Fig. 1.—Pregnancy rates for periods during which contraception was and was not practiced for a group of 991 women including 57 pathologic cases, and for the same group exclusive of the pathologic cases. (From an analysis of the preclinic fertility of women who subsequently attended a birth control clinic. Records on which this analysis was based were collected by the author.)

studied. Although the samples studied are small, the evidence is suggestive that this type of pregnancy wastage is probably unimportant in producing variations in fertility.^{9, 14, 21} Additional evidence from other studies confirms this finding (Table II). The proportion of pregnancies terminated by involuntary wastage is strikingly similar in all groups for which detailed information is available.

There is additional indirect evidence which makes it appear probable that involuntary factors are of little importance in causing variations in fertility. The incidence of dietary deficiencies, infection, and other diseases which may cause infertility probably varies inversely with economic status. However, infertility as expressed both in childlessness and in total number of children born varies directly with economic status. A high birth rate is found in precisely those groups in which

It was found that when the total exposure and pregnancies of 57 patients with known serious pathology were excluded from the tabulations, pregnancy rates, when contraception was not practiced, showed no decline with length of married life after the first pregnancy.* A sharp decline following the first pregnancy is probably due to the presence of periods of lactation and amenorrhea which may precede all pregnancies except the first. The rates are compared in Fig. 1 and Table I. The

TABLE I. PREGNANCY RATES PER 100 PERSON-YEARS' EXPOSURE WITH AND WITHOUT THE TOTAL EXPOSURE AND PREGNANCIES OF 57 PATHOLOGICAL CASES*

PERIOD OF MARRIED LIFE	RATES FOR PERIOD DURING WHICH CONTRACEPTION WAS NOT PRACTICED		RATES FOR PERIOD DURING WHICH CONTRACEPTION WAS PRACTICED	
	ALL WOMEN	PATHOLOGIC CASES EXCLUDED	ALL WOMEN	PATHOLOGIC CASES EXCLUDED
First pregnancy	271	304	41	42
Second and succeeding pregnancies				
Total	105	125	27	28
0-4	114	125	32	33
5-9	102	125	27	27
10-14	81	117	24	26
15-29	69	131	15	16

*From an analysis of the preclinic fertility of 991 women who subsequently attended a birth control clinic. Records on which this analysis was based were collected by the author.

same women could and, for the most part, did have exposure with and without contraception. Three findings are indicated from comparing the rates with and without the experience of these 57 women: (1) that the inclusion of the pathologic cases definitely lowered the rates among women who did not practice contraception, (2) that the influence of pathology on these pregnancy rates increased with age (length of married life), and (3) that the use of contraceptives had so marked an effect in itself in lowering pregnancy rates that the absence or presence of pathology in the proportion in which it appeared in the exposure during which contraception was practiced did not affect pregnancy rates significantly. These tabulations relate to a small and highly selected group of women, but they suggest the possible influence of pathology on pregnancy rates.

*The pregnancy rates represent pregnancies per 100 person-years' exposure to risk of pregnancy. A woman is presumed to be exposed to the risk of pregnancy if she is between menarche and menopause, living with her husband, and (1) all separations of husband and wife, (2) the actual number of months of gestation for each pregnancy plus a month or a fraction of a month for the puerperal period following it, and (3) the period following menopause or sterilization. The time remaining is the total exposure to risk of pregnancy, and pregnancy rates have been computed by the following formula:

Rate = $\frac{P}{Y} \times 100$, where P = number of pregnancies, and Y = number of years of exposure to risk of pregnancy. The rates represent the total experience of all women in the specified duration of married life and type of exposure, before attendance at a birth control clinic.

The types of contraception reported were mainly condom, coitus interruptus, douche, and alternations of these methods. The rates for the exposure during which contraception was practiced refer to the combined exposure with all types of contraception. Detailed studies of the relative effectiveness of these types of contraception have been previously published.^{7,8}

the types of pathology which might lead to infertility are most prevalent. It has been shown that in the small group studied the presence of pathology reduced the pregnancy rates of women who practiced no contraception. Therefore, to the extent to which couples practice no contraception, involuntary factors probably do reduce fertility and are at least partially responsible for the reduction in fertility with advancing age. Conversely, it is possible that relatively infertile couples find no need to practice contraception. The whole problem is exceedingly complex and can be summarized more easily after we have considered the importance of voluntary control as a cause of variations in fertility.

Voluntary control of fertility expresses itself in three ways: (1) in the practice of contraception, (2) in resort to induced abortion, and (3) in variations in frequency of coitus. Recent researches under the auspices of the Milbank Memorial Fund have shown the importance of voluntary control of fertility in producing variations in the birth rate. Professor Raymond Pearl, in his study of 30,000 women who came to hospitals to bear children, found no significant differences in age specific pregnancy rates by social class or color among women who had never practiced contraception. In his second progress report on part of his data,³ he showed that the prevalence and effectiveness of contraception were directly correlated with economic status in the group studied, and that the differences in pregnancy rates in that group were the result of these variations in contraceptive practice. Pearl estimates on the basis of his findings that 50 to 60 per cent of white married couples in cities east of the Mississippi and north of the southernmost tier of states practice contraception more or less regularly.

Contraception reduced pregnancy rates in Pearl's group by about 20 to 30 per cent,⁴ even when inexpertly and intermittently practiced. In the New York study previously cited,⁵ it was found that all contraception as practiced before contact with a birth control clinic reduced the risk of pregnancy by about 75 per cent. Both of these figures relate to pregnancies in a given period of exposure to the risk of pregnancy. A more realistic method of expressing the effectiveness of contraception as practiced by the New York sample is to compare the total pregnancy rate for the first ten years of married life, which includes time pregnant as well as time exposed, for women who did and did not practice contraception from marriage. All pregnancies, including those planned, are included in the rate of the group which practiced contraception. The pregnancy rates were just twice as high for women practicing no contraception as for those who practiced contraception from marriage (Table III). In other words, women who practiced no contraception had about twice as many pregnancies in the same period of time as did women who practiced contraception.

Illegally induced abortion appears to be of some importance in reducing the birth rate. It is impossible to estimate the prevalence of illegal

TABLE II. OUTCOME OF PREGNANCIES FROM HISTORIES OF WOMEN IN VARIOUS AREAS OF THE UNITED STATES

SOURCE OF DATA	YEAR OF STUDY	NUMBER OF PREGNANCIES	PER CENT OF TOTAL BY TYPE OF TERMINATION					
			TOTAL	LIVE BIRTHS	STILL-BIRTHS	TOTAL	ABORTIONS	
							SPONTANEOUS*	ILLEGAL
Pregnancies previous to one reported on survey: New York City ¹⁴	1935-1936	1,525	100.0	85.4	2.6	12.1	9.2	2.9
Previous pregnancies and current hospital births: Chicago (white multiparae) ¹⁵	1931-1932	5,840	100.0	86.7	13.3†		---	2.1
New York City (white multiparae) ¹⁶	1931-1932	7,686	100.0	85.0	15.0†		---	3.2
Pregnancy histories of patients seeking contraceptive advice: New York City ⁹	1932-1933	3,106	100.0	69.4	1.3	29.3	7.2	22.1
Cincinnati**	1935-1937	7,289	100.0	81.0	2.2	16.8	8.9	8.0
Baltimore ^{17, 18}	1927-1932	6,441	100.0	84.4		15.6	10.1	5.6
Minneapolis ¹⁹	1931-1935	8,875	100.0	82.5	1.3	16.2	10.7	5.5
Newark ²⁰	1928-1930	8,314	99.9	77.4	1.2	21.3	9.7	11.6
Philadelphia†	1925-1936	1,221	99.9	82.8	1.2	15.9	10.7	5.2§

*Includes therapeutic abortions, except as indicated.

**Unpublished data from studies of the Milbank Memorial Fund.

†Unpublished data from the private practice of Dr. Lovett Dewees, analyzed by Gilbert Beebe. Personal communication.

‡The proportion of abortions among the current hospital births is almost certainly much lower than among pregnancies in the general population, since the hospitalized abortions will be chiefly those accompanied by a definite morbidity and therapeutic abortions. It may be estimated that the wastage among *previous* pregnancies of these women would be about 18 per cent for the New York women and 16 per cent for the Chicago group.

§Includes therapeutic abortions and 1.1 per cent unspecified abortion.

riage which took place from one to twenty-five years before the interview is subject to wide error. However, it was assumed that this would be somewhat more accurate than the reporting of any other coital frequency except that at interview. A tabulation of the mean interval between marriage and the first conception by coital frequency, when no contraception was practiced, is shown in Table IV. There is a slight

TABLE IV. MEAN NUMBER OF MONTHS BETWEEN MARRIAGE AND FIRST CONCEPTION FOR WOMEN PRACTICING NO CONTRACEPTION, BY COITAL FREQUENCY IMMEDIATELY AFTER MARRIAGE*

COITAL FREQUENCY IMMEDIATELY AFTER MARRIAGE	NO. WOMEN	MEAN NO. MONTHS BEFORE CONCEPTION
Total	479	4.4
Once a week or less	45	4.6
Two to three times a week	212	4.7
Four to six times a week	121	4.3
Seven times a week or more	101	3.7

*From an analysis of the preclinic fertility of 991 women who subsequently attended a birth control clinic (pathologic cases included). Records on which this analysis was based were collected by the author.

but not significant shortening of the interval with increasing coital frequency. A study of post-clinic pregnancy rates by coital frequency at interview showed little or no relation between coital frequency and pregnancy rates since, although the information on coital frequency was probably relatively accurate, all the couples studied were practicing contraception of varying types and with varying degrees of effectiveness at that time. It appears that coital frequency has little or no effect on variations in fertility, but conclusive evidence on this point must await more accurate and extensive study.

All available data point to contraception and induced abortion as the most important causes of variations in fertility. Fig. 2, based on the same series of records, shows pregnancy rates for four successive periods of married life. The rates for each period are broken down to show the proportion of each type of pregnancy result. The pregnancy rates declined with increasing length of marriage, mainly because of the increasing practice and effectiveness of contraception in each successive period of married life. The birth rates declined even more rapidly than the pregnancy rates because of the increase in criminal abortion.¹³ Involuntary pregnancy wastage had little effect on the birth rate and did not vary with length of married life.

Research now in progress should give us new and valuable information on the physiology of reproduction. Until we know more about this subject, the interpretation of material concerning involuntary infertility will be difficult. Hartman's studies of ovulation in monkeys, showing, among other things, the frequency of anovulatory menstruation in these animals, impress us anew with our lack of knowledge concerning human ovulation. In the field of endocrinology, interesting work is being done in many sections of the country which is adding greatly to our knowl-

abortion in this country, since, being a criminal offense, it is not reported. Taussig¹⁰ estimates one abortion to 2.5 births in urban areas and one abortion to 5 births in rural areas. Recent studies indicate that the estimates for urban areas are probably high, since they are based on the preclinic records of women who attended the same New York birth control clinic for which data are included in Table II. Their induced abortion rates appear to be abnormally high when compared with those of groups unselected with respect to an interest in controlling their fertility, or with those of patients of birth control clinics in other urban areas (Table II). Estimates based on material from all sources indicate

TABLE III. PREGNANCY RATES PER TEN YEARS OF MARRIED LIFE FOR WOMEN MARRIED 0-9 YEARS*

ORDER OF PREGNANCY	NO CONTRACEPTION PRACTICED			CONTRACEPTION PRACTICED†		
	YR. MAR.	NO. PREG.	RATE	YR. MAR.	NO. PREG.	RATE
Total	452.3	307	6.8	2218.9	747	3.4
First pregnancy	121.3	106	8.7	620.0	320	5.2
Second and succeeding pregnancies	331.0	201	6.1	1598.9	427	2.7

*From an analysis of the preclinic fertility of 991 women who subsequently attended a birth control clinic (pathologic cases included). Records on which this analysis was based were collected by the author.

†Includes interruption of contraceptive practice for planned pregnancies.

that a total rate of 18 abortions (spontaneous and induced) per 100 live and stillbirths is probably a more accurate figure.¹⁵ Millar's studies in Cincinnati¹¹ show that the abortion index increased much more rapidly than the birth index, in the group studied, between 1918 and 1932. A study of the proportion of pregnancies terminated by illegal abortion in the New York group cited above showed that nearly one-fourth of all pregnancies were so terminated. The proportion of pregnancies terminated by illegal abortion increased directly with length of married life, and increasing order of pregnancy, and varied with income and religion.^{9, 21} The incidence of illegal abortion in this group is probably very much higher than in an average unselected population group, but resort to induced abortion appears to vary with order of pregnancy and social and economic status in other groups for which detailed information is available.^{12, 14, 21}

There are no reliable data on the relation of coital frequency to variations in fertility. This is probably partially due to the fact that couples do not know their average frequency of coitus. Reliable data have been obtained for a few couples from calendar records kept by those couples over a period of months or years. These have been made mainly in connection with isolated studies of sterility and of the so-called "safe period" and have not been correlated with fertility. In the New York clinic study previously cited, the women interviewed reported coital frequency immediately after marriage and at the time of the interview. Obviously, the reporting of coital frequency immediately after a mar-

SUMMARY

1. Recent scientific interest has been directed toward determining the causes of variations in the birth rates, since present differentials indicate that our future population will be recruited largely from agricultural and urban laboring classes.*

2. The incidence of involuntary sterility and infertility in selected population groups is unknown. Study of a small, selected group suggests that the increasing incidence of pathology with advancing age is an important factor in the decline in fertility, when contraception is not practiced.

3. The incidence of involuntary pregnancy wastage, in a selected group of women, shows no change with age or religion and has been approximately the same for the past twenty-five years.

4. Voluntary control of fertility by means of contraception and induced abortion is responsible for major variations in pregnancy and birth rates.

5. Further researches on the physiology of fertility and the incidence of sterility are needed before the causes of variations in fertility can be adequately interpreted.

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*The occupational groups on which these studies are based are a slightly modified form of the occupational code used by the United States Bureau of the Census in 1920.

edge of the physiology and pathology of fertility. These researches have been largely confined to animal experimentation, but it is to be hoped that some of the techniques contrived will be applicable to human study before long.

Comparatively little is known concerning the physiology of reproduction, and even less is known about the effect of pathology in producing infertility. Information concerning the latter might be obtained by enlisting the support of a group of obstetricians and gynecologists who would be willing to keep simple, uniform fertility histories in connection with medical histories. Such a series of records might yield valuable information concerning the relative incidence of sterility or infertility in relation to certain pathologic processes. For example, in addition to knowing what percentage of sterility cases was due to tubal infec-

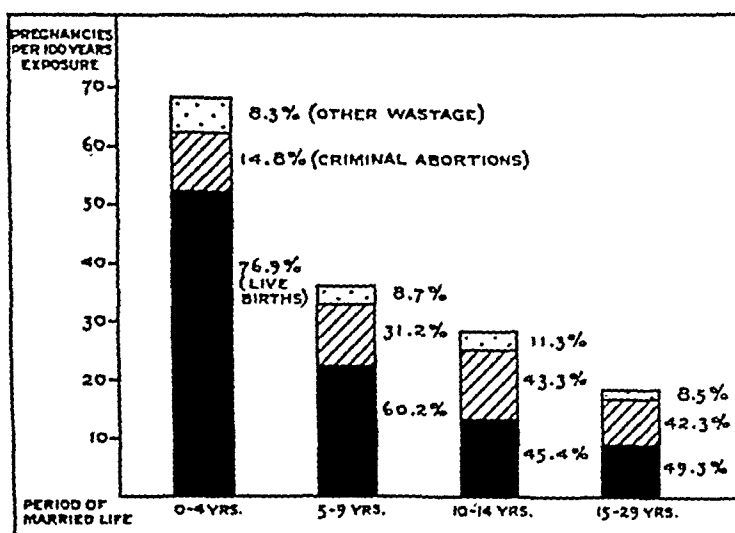


Fig. 2.—Pregnancy rates and distribution of pregnancy terminations by type in specified periods of married life. (From an analysis of the preclinic fertility of women who subsequently attended a birth control clinic. Records on which this analysis was based were collected by the author.)

tion, it would be possible to learn how frequently sterility or infertility is found in a known number of cases of tubal infection—a question which needs to be answered for all types of pathology. In addition to such a study, it is important that further studies of contraceptive practice and abortion be made in selected population groups of types different from those already studied.

A great deal of further research must be done before we know very much about the medical aspects of fertility. The study of the problem has been somewhat neglected by the medical profession until recently, but it is to be hoped that the recent awakening of interest on the part of a number of prominent physicians will furnish the impetus for further research in this field. Such researches are of vital importance to a positive attack on the problem of a falling birth rate.

That the reverse of this positive significance of hormonal tests is *not* necessarily valid, is demonstrated by a case quoted by Schumann in a discussion of Kimbrough's paper,⁵ in which chorionepithelioma developed six months following a supposed miscarriage, although repeated hormonal tests in the interim had been negative.

Huberman, of Newark, recently reported a similar case to the Society of Surgeons of New Jersey.

We have delivered in this hospital up to the first of March, 1936, 20,450 living babies. We had 15 cases of hydatid mole, which is an incidence of one in 1,333 full-term deliveries. This is well within the widely divergent statistics of incidence from various sources. The incidence in terms of all pregnancies is impossible to estimate, because, although it is unquestionably much higher in relation to early abortions than it is to late pregnancies, our material here includes so few abortions as not to represent in any sense a cross-section of all pregnancies.

Schumann has long since pointed out the difficulty of arriving at any estimate of incidence referable to all pregnancies.

This does, we believe, represent the true incidence of material coming under our purview, inasmuch as every conception product, including abortion products, moles of all kinds and mature placentas, is subjected to careful gross and microscopic scrutiny in our laboratory.

Detailed analysis of this series shows the following data:

Age.—Youngest eighteen years, oldest 40 years, average 27 years. The majority were well in the fourth decade of life.

Race.—All except one occurred in white patients.

Parity.—In one-third of the patients the mole represented the first pregnancy; in the oldest individual in the group it was the ninth; for the majority it occurred in the third or fourth pregnancy.

Miscarriages.—Only two of the group had previous miscarriages and each of them had only one.

Subsequent Births.—Three of the group have had one later pregnancy and one has had two.

Symptoms Prior to Determination.—With two exceptions every case presented bleeding. The majority had cramps or other types of pain associated with the bleeding. Bleeding varied widely in duration and amount prior to coming under observation. Two presented vomiting, dehydration or other symptoms of toxemia. One had intercurrent valvular heart disease. One was characterized by apparent arrest of pregnancy. Only three showed enlargement of the uterus beyond that consistent with the estimated duration of pregnancy. One showed marked diminution in the size of the uterus as compared with that consistent with the estimated duration of pregnancy. One only had passed, and noted, characteristic grape-like masses before coming under observation.

Admission Diagnosis.—In only 3 was hydatid considered first as an admitting diagnosis; only 1 other hydatid was considered secondary as an admitting diagnosis.

The others were primarily diagnosed as: 2 placenta previa, 1 abruptio placentae, and 1 missed abortion. All the others as inevitable or incomplete abortions.

Nature of Products Passed.—The size and weight of the moles varied greatly. Phrases used to describe them were somewhat indeterminate, as "large hydatid";

THE VALUE OF HORMONAL FINDINGS IN HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

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CHORIONEPITHELIOMA relatively is so rare a disease, that in approximately forty years since it was first described,¹³ there have been reported probably not more than two thousand cases, while in the past seven years, since Aschheim¹ first recorded the significance of hormonal tests in relation thereto, not more than two- or threescore cases have been reported in which hormonal tests have been correlated to this type of tumor.

No reports so far (March, 1936) appear to embrace more than three cases of early chorionepithelioma correlated to hormonal test findings.

A report of the three cases encountered in the past three years in this hospital therefore would appear to require no apology.

In 1929 Fels and Rossler, as quoted by Mazer and Edeiken,¹¹ concluded:

1. That in hydatid mole and chorionepithelioma there is much more prolactin secreted than in normal pregnancy.

2. The quantitative estimation of this hormone is an actual guide to diagnosis in that

3. Presence of increased hormone for more than *two weeks* after normal pregnancy, or more than *eight weeks* after the extrusion of hydatid, is *proof* of chorionepithelioma.

4. Persistence of positive test for this hormone *after* operation and removal of chorionepithelioma is *proof* of metastasis.

These conclusions appear to have obtained practically universal acceptance.

Brindeau and Hinglais² point out, while agreeing with other authorities, that the titer of prolactin in hydatid and chorionepithelioma is very much higher than in normal pregnancy, by factors variously estimated at from ten to several hundred times, the actual titer in individual cases of either of these conditions varying within wide limits, but always above that of normal pregnancy. The prognostic importance of the behavior of hormonal tests therefore depends on relative curvature. They find that after the evacuation of a mole, for instance, whether the original titer has been from 2,000 to 60,000 rat units per liter, there is a prompt drop to less than a thousand. If, however, chorionepithelioma were present at the same time or developed subsequently to the hydatid, there will be a secondary rise within thirty to fifty days, which rise tends to be progressive. The occurrence of this secondary rise is adequate basis for a diagnosis of malignancy and for radical extirpation of the affected organ.

Morbidity.—Ten of the 15 patients showed no morbidity whatever; 1 was febrile on admission but the fever stopped promptly with the passage of the mole, and the other 4 showed slight febrile reactions lasting from three to ten days.

Mortality.—There was no mortality in the entire group.

Postpartum Complications.—Two patients showed recurrent bleeding following the passage of the mole; 1 had severe secondary anemia and catarrhal jaundice; 1, severe anemia; 1, furunculosis of the back, and 1, vesicovaginal fistula following complete hysterectomy for chorionepithelioma.

Remarks.—All patients have been traced to the present time and are in good health now with the following exceptions: One is reported by a private physician to be in good general health but to have some type of undetermined ovarian pathology; 1 other has a slight ovarian enlargement; and 1 is now pregnant and in good condition.

Of the 15 cases of hydatidiform mole cited, 3 patients had chorionepithelioma. This is an incidence of 20 per cent of chorionepithelioma to all moles. As these are the only known cases of chorionepithelioma in our material, 100 per cent of our chorionepitheliomas have been preceded by moles.

Details of these three cases are as follows:

CASE 1.—(No. 13 of hydatid series.) (History No. 4181.) Patient, twenty-two-year-old white gravida iv. All prior history irrelevant except that almost two years before, an egg-sized freely movable mass had been noted in relation to the right vaginal fornix. Present pregnancy commenced Aug. 8, 1934. On Oct. 19, 1934, when two and a half months pregnant, had low abdominal pain, vaginal bleeding, and passage of a clot. She was admitted on the same date.

Because of continued bleeding and progressive anemia, dilatation and curettage was attempted Nov. 2, 1934; cervix was so rigid that this was not carried out, but a portion of tissue was digitally removed, which proved to be hydatid material. On Nov. 3, 1934, dilatation and curettage was accomplished with the removal of 700 gm. of hydatidiform tissue. She was given a transfusion of 500 c.c. of blood.

Friedman:

Positive 9th day after expulsion of mole to 5 c.c. of urine
Positive 23rd day
Positive 34th day
Positive 60th day

There had been 3 episodes of menstruation-like bleeding during the five weeks prior to her second admission, 54 days after removal of mole. Based entirely on the persistence of the hormonal reaction total hysterectomy was performed, sixty-eight days after removal of mole.

Examination showed a chorionepithelioma so completely imbedded in the myometrium that it would almost certainly have escaped detection by curettage.

Following hysterectomy:

Friedman—

Positive on 6th day
Negative on 9th day to 1 c.c. urine
Negative on 15th day to 5 c.c. urine
Negative 4½ months later
Negative 5 months later
Negative 15 months later (April, 1936)

"several pieces of hydatid tissue"; "500 c.c. of blood clot with hydatid tissue." Others were specified by definite weights: 80 gm.; 1,100 gm.; 2 ounces; 460 gm.; one uterus contained a well-formed six weeks' fetus, the placenta showing hydatidiform degeneration. Hydatid coexisted with missed abortion. One patient showed chorionepithelioma on curettage. One patient presented necrotic decidua, the hydatid characteristics of which were determined only by microscopic examination.

X-ray Findings.—In only four was the chest x-rayed prior to the termination of the condition, in all cases the result being negative for evidence of metastasis. Three patients showed no evidence of fetal parts by x-ray at a period of gestation when such parts should have been demonstrable by x-ray in normal pregnancy. The other patients had no x-ray examination.

Friedman Tests.—1. Friedman positive 11 and 29 days after passage of mole; no further Friedman observations but now reported in good health after three years.

2. Positive eight days after dilatation and curettage; negative fifteen days after; has had one normal pregnancy since and reported in good health.

3. Negative six and twenty-nine days after passage of mole; now reported in good health after four months.

4. Friedman negative and patient in good health at the present time, two years after passage of mole.

5. Positive before passage of mole and again twelve days later; negative seventeen and thirty-five days after passage of mole; now reported in good health more than two years later.

6. Negative seven days after passage of mole; positive thirty-four days after passage of mole and again negative thirty-seven days after passage of mole; reported in good health more than a year later.

This anomalous positive finding is not satisfactorily explained.

7. Positive in dilution up to 1:100 prior to hysterectomy; negative twenty-three days, again nineteen months postoperative; in good condition on physical examination at the present time.

8. No findings.

9. Questionable result eleven days after passage of mole; negative twenty-one days after passage of mole; positive three months after passage of mole; again positive three and one-half months after passage of mole. These positives were due to a succeeding pregnancy. This woman has had two living deliveries since the mole, the last March 25 of this year.

10. Negative eight days and thirty days after passage of mole; health good nine months later.

11. Positive five days and ten days after passage of mole; negative twelve days, nineteen days, and fifty-nine days after passage of mole. This patient is again pregnant, one and one-half years after passage of mole.

12. Positive four months prior to passage of a missed abortion; negative seven weeks later.

The other three cases were complicated by chorionepithelioma and will be separately discussed.

Operative Procedures.—Two patients expelled the mole completely without operative procedure; 1 was treated by abdominal hysterotomy for supposed abruption of the placenta; in 1 a supravaginal hysterectomy was done on a primary diagnosis of hydatid; in 3 others the conception product was removed by digital and forceps exploration of the uterus; and all the others were treated by dilatation and curettage.

bleed; bleeding increased and on Jan. 29, 1935, she began to have severe pain in back radiating to lower abdomen. She was admitted Jan. 30, 1935, four and one-half months pregnant; no fetal heart heard. On Jan. 31, 1935, she passed spontaneously a 460 gm. mole. Nonmorbid puerperium.

Friedman:

Positive 4 days after extrusion of mole

Negative 12 days after extrusion of mole

Negative 18 days after extrusion of mole

Negative 21 days after extrusion of mole

Thirty-three days after extrusion of mole, she bled for four or five days with passage of small clots. Friedman test was twice positive within two and a half weeks of this episode. Because of the repeatedly positive Friedman after it had



Fig. 3.—Case 2. Uterus with polypoid hemorrhagic masses filling the uterine cavity. Large lutein cyst of ovary.

been negative for several weeks, total hysterectomy with bilateral salpingectomy and right oophorectomy was performed, March 21, 1935. A chorionepithelioma was found. The Friedman test was negative and her general condition was good March 28, 1936, more than twelve months later.

Acknowledgment is made of the privilege of reporting this case from the private service of Dr. Charles B. Kelley.

It is hoped that failure of metastasis to occur in these two cases, twenty-six and twenty-three months, respectively, after removal of tumors of a type notoriously rapid in metastatic development means definite cure.

CASE 3.—(Fifteenth in hydatid series.) (History No. 25435.) Patient, thirty-one-year-old white, gravida ii. Her previous history was irrelevant, except habitual menstrual irregularity. Present pregnancy commenced Aug. 22, 1935. On Dec. 15, 1935, passed painlessly a large blood clot, and on Dec. 21, 1935, passed another

Patient is now well, February, 1937, except that the right ovary is enlarged to about three times normal size, but this condition was apparently noted before the mole conception.

X-rays of chest for metastasis were negative April 1, 1936, and February, 1937.



Fig. 1.—Case 1. Chorionepithelioma of uterus, completely embedded in the musculature of fundus; does not reach the endometrium or the serosa; curette would not have revealed it.

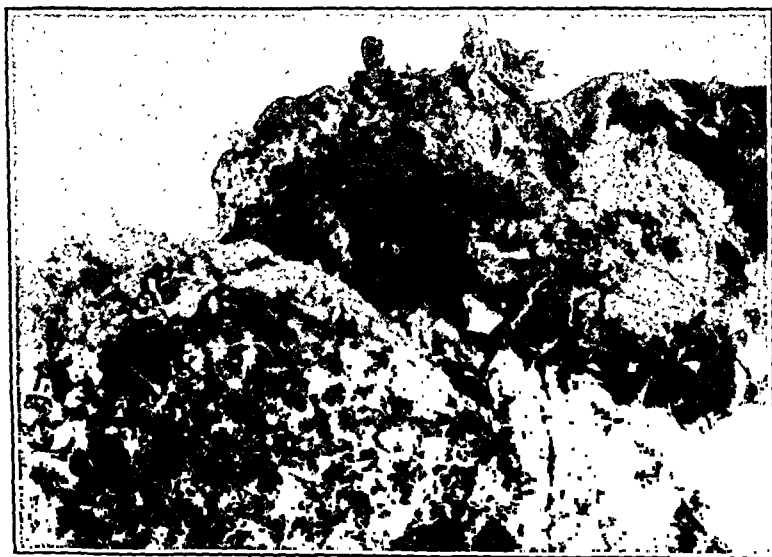


Fig. 2.—Case 2. Hydatidiform mole preceding chorionepithelioma. Cysts are thin-walled and whole tumor shows extensive hemorrhagic degeneration and necrosis.

CASE 2.—(No. 14 of hydatid series.) Patient, a thirty-seven-year-old, white, gravida iv. (History No. 18448.) Prior history irrelevant except one miscarriage. Present pregnancy commenced in September, 1934. On Jan. 23, 1935, she began to



Fig. 5.—Case 3. Diffuse growth of chorionepithelioma invading the entire wall of fundus. Hemorrhagic portions have broken through endometrium.

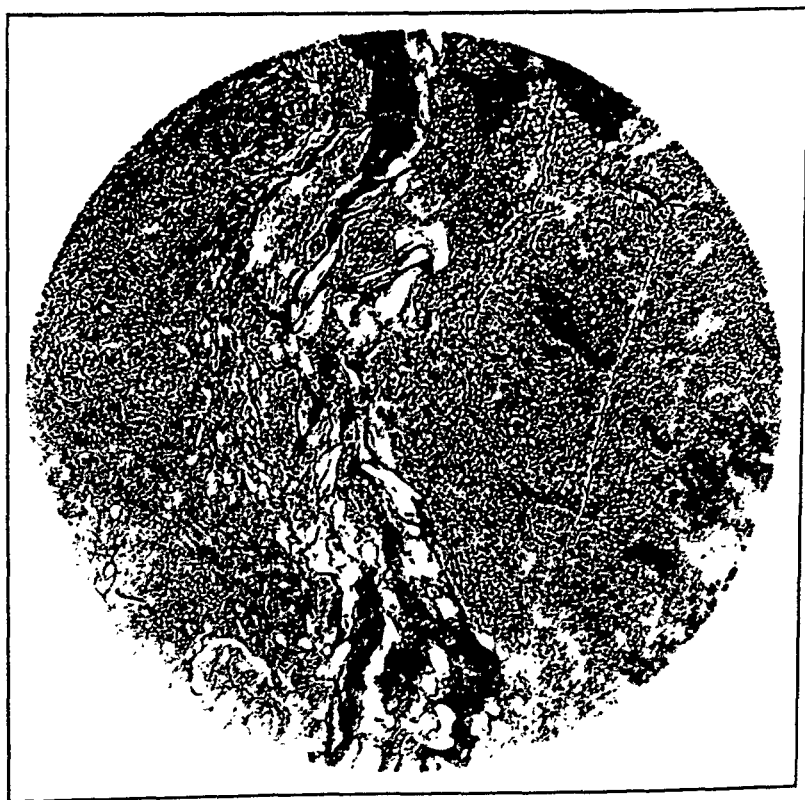


Fig. 6.—Case 3. Microphotograph from hemorrhagic and necrotic portion of chorionepithelioma as seen in Fig. 5.

clot which looked like grapes; Jan. 15, 1936, passed two cluster-like clots and one mass, size of an orange; admitted same date, slightly febrile, almost five months pregnant. On Jan. 16, 1936, 75 gm. of degenerated chorionic villi were removed by curettage; this and the orange size mass were found to be hydatid.

Friedman:

Positive 8th day

Positive 34th day

Positive 37th day

In the meantime there had been two episodes of bleeding, one of ten days' and one of two weeks' duration. Diagnostic curettage was done March 9, 1936, thirty-five days after extrusion of mole, and showed chorionepithelioma. X-ray at this time was negative for chest metastases. Complete hysterectomy was performed March 12, 1936, fifty-seven days after extrusion of mole. Pathologic examination



Fig. 4.—Case 3. Hydatidiform mole preceding chorionepithelioma. Cysts of irregular size, with extensive hemorrhage and necrosis.

of uterus confirmed presence of chorionepithelioma in fundus. Friedman: Negative March 26, 1936, April 11, 1936, and October, 1936.

This patient has been followed to the present, February, 1937, eleven months after hysterectomy and is completely well to date.

This brief review of 15 cases of hydatid mole, including 3 cases complicated by chorionepithelioma, demonstrates that in all cases the behavior of the hormone tests has been consistent with the clinical history. In two cases the hormone tests have determined early radical treatment. In one of these positive diagnosis even by exploratory curettage would have been impossible, and failure to recognize the significance of the hormonal test would have deprived the patient of early and curative treatment.

We have continued to use paraldehyde with nembutal or sodium amytal, routinely, except in cases of primary inertia, some of the more serious complications of labor or in cases requiring the mother's cooperation as in a test of labor following a previous cesarean section.

We are still impressed with the desirability of withholding amnesia in primiparas until the cervix is well thinned out and dilated at least 4 or 5 cm., the head well fixed in the pelvis and the pains coming at intervals of three to four minutes. If some relief is needed prior to this, the administration of $\frac{1}{6}$ gr. of morphine, with $\frac{1}{300}$ gr. of scopolamine, by hypodermic, or the use of $1\frac{1}{2}$ gr. of nembutal, or 3 gr. of sodium amytal, will usually suffice.

In multiparas, also, we believe it is desirable to withhold amnesia until the head is fixed in the pelvis, the cervix fairly thin and dilated 2 to 3 cm., and the pains four to five minutes apart. Damon² in a recent article on pentobarbital-scopolamine amnesia in labor, also emphasizes the desirability of withholding the drugs until labor is well under way.

It would be unfortunate indeed, if, either through insistence on the part of the patient or over-indulgence on the part of the physician, amnesia should become an early first stage procedure, when pains are still irregular, the cervix uneffaced or the head still movable. Under such circumstances the physician would frequently be faced with the necessity of exceeding the recommended dose, permitting the patient to awaken undelivered or undertaking a more difficult operative delivery necessitated by the resulting inertia.

A more dependable and complete amnesia may be obtained if paraldehyde is preceded one to two hours by 3 gr. of nembutal, or 6 gr. of sodium amytal. In this respect no change has been made in the technique. If rapid action is desired, the contents of the capsules dissolved in one ounce of water, may be given twenty to thirty minutes preceding paraldehyde.

However, our method of administration of paraldehyde has been changed from rectal to oral in the great majority of cases. The principal reason for this change has been the occurrence, in several cases, of undoubted trauma to the upper rectum or lower sigmoid from the impact of the rectal tube in the attempt to inject the olive oil-paraldehyde solution sufficiently high to insure retention and rapid absorption. Even with the use of a fairly soft rectal tube and care in manipulation, trauma to the bowel wall may occur, as evidenced by tenesmus, localized pain and induration over the sigmoid and moderate fever, coming on four or five days after delivery. The condition has fortunately subsided within a few days but is nevertheless an unnecessary discomfort to the patient and worry to the attendant. The oral method is simpler, more easily intrusted to a nurse and is more rapid in action.

We have found that the great majority of patients willingly take paraldehyde by mouth, especially if they are already somewhat drowsy

As indicated above, laboratory findings must not be regarded as wholly determinative in these cases. If they are positive they confirm the significance of the clinical behavior. Negative findings, however, cannot be implicitly relied upon as in all departments of medicine but, the principal basis of diagnosis and treatment must continue to depend upon history, course, clinical findings, and the common sense and surgical training of the attendant.

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IMPROVEMENTS IN THE PARALDEHYDE METHOD OF RELIEF OF PAIN IN LABOR

AN ANALYSIS OF 500 CASES

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SINCE the publication of our initial experience with paraldehyde as a basic agent for relief of pain in labor¹ development of certain helpful modifications in the technique has prompted us to summarize our more recent impressions of, and experience with this method.

Furthermore, in view of the outspoken criticism it behooves those who are already using established methods of relief of pain, or pioneering new methods, to justify the procedure by a frank and unbiased statement of results. If the method helps the expectant mother to face the coming ordeal of labor with less fear and apprehension, does not increase operative obstetrics, maternal or fetal morbidity or mortality and avoids the nervous shock frequently resulting from comprehension of the realities of labor, there remains no valid argument against its use. A physician's service to his patient in labor may vary from constant attendance throughout labor to a brief attendance at the actual delivery, but to those of the profession who remain with the patient throughout labor, there are probably very few, now using amnesic agents, who would be willing to go back to the former inadequate means of relief and be forced to endure the pleas of both the patient and family, to take some action which is often contrary to the best obstetric judgment.

almost all cases and consider it an essential requirement. Patients occasionally remember the wrists having been restrained, even though they have no memory of the labor pains.

It has been our experience as well as that of others that in many cases a short period of moderate inertia occurs soon after the administration of paraldehyde. It is manifest in a slowing of the pains from three- or four-minute to five- or six-minute intervals but seldom continues more than one hour. It is a help rather than a disadvantage, for it enables the state of sleep and amnesia to be established with less disturbance by the pains.

Stimulation of the pains is not necessary unless the inertia persists for more than one hour after the patient is asleep. Herein lies the importance of withholding the paraldehyde until the character of the pains, condition of the cervix, and descent of the head, indicate that labor is well established. If used too early in labor, this period of inertia will tend to be prolonged, persistent and more difficult to overcome. We have made frequent use of artificial rupture of the membranes just preceding the administration of paraldehyde or just after amnesia is fully established, to further insure efficient pains and good progress. This has proved to be a helpful and harmless procedure, provided the head is fixed, the cervix thin and dilated 4 to 5 cm., and the pains occurring at three- to four-minute intervals.

In the majority of cases there is a spontaneous increase in the frequency and strength of the pains within one hour. If inertia persists beyond this period, several drops of pituitary extract should be instilled onto the nasal mucous membrane, using a hypodermic syringe as a dropper. This is preferable to plugging the nostril with cotton saturated with pituitary extract, as it is less likely to irritate or arouse the patient. There is a definite effect within five to ten minutes, but one practically never encounters the severe type of reaction, with prolonged tonic contraction and slowing of the fetal heart sounds that is likely to occur with the subcutaneous administration. There would undoubtedly be greater safety for both mother and baby if the intranasal, rather than the subcutaneous administration of pituitary extract were more generally used during labor. In many cases not more than one intranasal instillation of pituitary extract is necessary, the pains continuing with normal frequency and strength to the end. The patient makes bearing down, expulsive efforts in the second stage with almost the same efficiency as if she were awake.

Restlessness during or between pains may seriously interfere with preparing and draping the patient for delivery and controlling her during crowning of the head. This has been overcome by a modification in technique which we have found to be safe and most satisfactory. Ether, a mask, and a sterile towel are kept conveniently at hand in the labor room. When crowning has begun and the head remains slightly

from the administration of nembutal or sodium amytal during the preceding one or two hours. The initial dose of six drachms (24 c.c.) is stirred well in about two ounces of cold water. The patient should be raised to a sitting position in bed. Not more than a swallow should be taken at first, followed by a small piece of orange. If vomiting occurs, due to dislike of the drug or to having taken food too recently, it will occur usually within five minutes and very little of the dose will thus be lost. The stomach then being empty, or if no vomiting has occurred within five minutes, further swallows are taken at intervals of several minutes, until the entire dose has been taken within a period of fifteen to twenty minutes. The patient begins to sleep and amnesia is already present by the time the last swallow has been taken.

Subsequent doses of one to two drachms (4 to 8 c.c.) may be necessary if vomiting occurs or if the behavior or conversation of the patient indicates returning consciousness. The total dose rarely exceeds six to eight drachms (24 to 30 c.c.) of paraldehyde preceded by 3 gr. of nembutal or 6 gr. of sodium amytal. Should vomiting be persistent, it may then be necessary to administer paraldehyde in olive oil by rectal injection.¹ To lessen the possibility of vomiting, it is well to caution the patient to eat very lightly, if at all, at the onset of labor.

An objection most frequently mentioned, in opposition to amnesia during labor, is the troublesome degree of restlessness which is sometimes seen. It is most pronounced in patients of a highly nervous or excitable temperament, but it must be remembered that patients of this type are noisy and restless without any medication. Large doses of barbiturates accentuate this reaction. It is only logical, however, to expect it to occur to some extent in any method of amnesia, as a natural reaction to painful stimuli, unchecked by any voluntary control.

With paraldehyde as a basic amnesic agent, using only a small dose of barbiturate, such cases of exaggerated motor or psychic activity occur in only a small percentage of patients and may be controlled by a dose of morphine. Exceptionally, it may be necessary for the attendant to desist from all further attempts to maintain amnesia and endeavor to arouse the patient as soon as possible.

The uncertainty as to a patient's behavior, while in an amnesic state, makes it necessary to have a nurse or dependable assistant with the patient throughout labor. Her task of controlling a patient who shows some degree of restlessness during labor is rendered much simpler and the patient is protected from chance of self-contamination of the vulva or injury, by the use of wrist pads and restraining leather cuffs fastened to each side of the bed by which the movement of the arms is restricted and the patient kept on her back. The eyes are not covered or the wrists restrained until at least one hour after the dose has been given, and the patient thoroughly asleep. We use this degree of restraint in

seems best in such cases to give coramine at birth to stimulate crying and aid in full expansion of the lungs. The infant should be turned to the lateral or prone position with the foot of the crib raised somewhat, to facilitate drainage of mucus from the air passages. Aside from drowsiness, the first twelve to twenty-four hours after birth the babies show no difference in nursing, behavior, gain in weight, etc.

To protect the patient from possible harm, should she awaken in a dazed condition some hours after delivery, our former routine was to place the bed against the wall and fasten a chair to the opposite side. More recently we have been using a belt consisting of a strip of unbleached muslin four inches wide and sufficiently long to permit clamping each end to the metal structure of the bed. To the center of this strip is sewed a strip of the same material and width which is buckled about the patient's waist. This permits turning from side to side but does not allow her to roll to the edge or get out of bed. It is removed as soon as she has awakened and is rational.

As the effect of the drugs begins to wear off after some hours, the return to consciousness may occasionally be accompanied by restlessness or emotional disturbance, until the patient is fully awake. It has been found most helpful to administer $\frac{1}{6}$ gr. of morphine by hypodermic injection at the first evidence of restlessness or returning consciousness. This insures a longer period of rest and quiet, from which the patient awakes fully conscious and rational. The family should not be allowed to disturb the patient during this period of rest.

Analysis of the last 500 consecutive cases in which paraldehyde was used shows that complete amnesia was obtained in 92.6 per cent and partial amnesia in 6.2 per cent. Since the "islands of memory" of the latter group concern events of little significance to the patient and carry no recollection of pain, we are justified in stating that complete amnesia as to pain, may be obtained in 98.8 per cent. Failure was noted in 1.2 per cent. This represents a very low incidence of idiosyncrasy or resistance to the usual effects of the drug.

The average duration of amnesia before delivery was five hours and twenty-four minutes in nulliparas and three hours and eighteen minutes in multiparas. The average duration of sleep after delivery was four hours and forty-eight minutes in nulliparas and five hours and thirty-six minutes in multiparas. The hours of sleep during and after labor account for the feeling of rest and well-being so frequently noticed when these patients react.

The total duration of labor was thirteen hours and eighteen minutes in nulliparas and eight hours and fifty-four minutes in multiparas as compared to sixteen hours and thirty minutes in nulliparas and eight hours and forty-five minutes in multiparas under the former routine of nembutal-morphine, nitrous oxide and ether.

visible between pains in the multipara, or has produced slight tension on the perineum in the nullipara, ether is dropped onto the mask held high enough over the patient's face to avoid choking or realization that ether is being administered. Careful induction of anesthesia is necessary to avoid memory of this event and imperfect amnesia. Within a few minutes the mask may be lowered to the patient's face and the stage of primary anesthesia reached. Meanwhile the nurse should have finished scrubbing by the time the patient is anesthetized and moved to the delivery room. The head may be held back with the sterile towel should it progress too rapidly before anesthesia is established. While the nurse is preparing and draping the patient, the physician scrubs and is gowned and gloved. Only a small amount of ether is given while the patient is being prepared for delivery. She is relaxed and quiet and there is no interference with the preparation. Pains usually recur by the time the patient is draped and delivery occurs spontaneously, aided, if necessary, by episiotomy or hypodermic administration of two or three minims of pituitary extract.

By this method it is possible to carry out an orderly obstetric technique, protect the patient from contamination, permit a natural birth in the majority of cases and lessen the physical strain on the part of the attendants. For those who prefer to do routine low forceps delivery, it further simplifies the forceps delivery and lessens the extent of the episiotomy.

The placenta is usually ready to be delivered by simple expression in seven to eight minutes and there is no tendency to postpartum hemorrhage. As a precautionary measure, however, it is best to give one of the newer ergot preparations by hypodermic injection, immediately after delivery of the placenta.

In our first report, it seemed that the degree of interference with prompt establishment of the infant's respiration and cry at birth was negligible. However, with further experience with the method and the use of some additional ether just before delivery, according to the technique above described, we have noted a tendency to a short period of apnea after birth and some sluggishness in the establishment of regular breathing and vigorous crying in 12 per cent. The condition would seem to be due rather to a state of drowsiness, than to a specific depression of the respiratory center. If morphine has been administered within three or four hours before delivery, this behavior is more likely to be noticed.

In full-term normal babies, some degree of apnea or sluggishness apparently has no detrimental effect, as a little stimulation by spanking or gentle mouth to mouth inflation of the lungs promptly establishes good respiration and crying. It is probably true, however, that with premature infants, this sluggishness may predispose to atelectasis. It

In our first report on paraldehyde there was no fetal mortality in the series of 100 cases under paraldehyde, and no fetal mortality in the series of 100 patients delivered prior to the use of paraldehyde. In the present series of 500 cases the uncorrected fetal mortality was 1.8 per cent. Analyzing the nine natal or neonatal deaths, we have eliminated a case of hydrocephalus delivered by craniotomy, a premature infant weighing $3\frac{3}{4}$ pounds, a case of abruptio placentae in which the fetal heart sounds ceased early in labor before paraldehyde was administered, and a stillbirth apparently due to premature rupture of the membranes, intrapartum infection (103° F.), prolonged labor, contraction ring, and difficult midforceps delivery. The corrected fetal mortality is 1 per cent. computed from the following cases:

A slightly premature infant (eight and one-half months) which died one hour after delivery, clinical and autopsy diagnosis, atelectasis; a full-term infant delivered by low forceps following persistent and increasing slowing of heart sounds, apparently due to pressure on a coil of cord around the neck; a slightly premature infant (eight and one-fourth months) which died one hour after delivery, clinical and autopsy diagnosis, atelectasis; a premature infant (5 pounds 7 ounces) which lived two days, clinical diagnosis, atelectasis; and a premature infant (eight and one-fourth months) which died six hours after birth, clinical diagnosis, atelectasis.

On the basis of this low natal and neonatal mortality (1 per cent), it may be said that paraldehyde has no harmful effect on full-term normal infants. If used in cases of premature labor, the administration of coramine may be advisable at birth, to aid in full expansion of the lungs and lessen the possibility of atelectasis.

As mentioned in our first report, there seemed to be no contraindications to the use of this method in home confinements. This has been verified by reports from several general practitioners in small communities who have been using it with very satisfactory results.

To summarize our more recent experience with paraldehyde in labor, we believe that complete amnesia as to pain can be obtained in fully 98 per cent of cases; that the technique has been simplified by oral administration of the drug; that facilities for restraint of the patient's wrists to the side of the bed should be available, to better protect the patient and lighten the duties of the attendant; that pituitary extract dropped into the nose is a valuable and safe aid in overcoming any prolongation of a temporary inertia; that control of the patient for final cleansing, draping and delivery is greatly facilitated by the induction of light primary ether anesthesia during crowning of the head, just before moving the patient to the delivery room; that a mild degree of apnea or sluggishness in breathing or crying is to be expected in about 12 per cent of full-term, normal babies but is of no serious significance and is easily overcome, and that if paraldehyde is given in premature

Excitement under the paraldehyde method is defined as constant motor and psychic activity, both during and between pains manifested by loud outcry, and efforts to sit up or get out of bed. It occurred in 2.8 per cent. A dose of pantopon or morphine is of great benefit in these cases. Restlessness is defined as a moderate degree of psychic and motor activity, present during, but not to any troublesome extent between, the pains. It occurred in 7.2 per cent. In attributing restlessness and excitement to the drugs used, in fairness we should remember that the same reactions are noted as frequently in labors conducted without drugs, in patients of a certain type. To most attendants and families noise and restlessness are better endured if there is assurance that the patient does not realize what she is doing and will have no recollection of it.

A moderate degree of uterine inertia was noted in 12.8 per cent, as compared to 13 per cent without paraldehyde. We refer to persistent inertia rather than to the short temporary inertia which occurs so frequently immediately after administration of the paraldehyde. The figures, therefore, do not indicate any troublesome degree of inertia with paraldehyde, and the intranasal use of pituitary extract, when indicated, will be found to be both adequate and safe.

Under our former method of relief of pain in labor, morphine was used more frequently and fetal apnea at birth occurred in 17 per cent. Under the paraldehyde method, apnea at birth was noted in 11.6 per cent. It appears to be due to a state of drowsiness rather than to a specific depression of the respiratory center and responds easily to mild stimulation or a few gentle mouth to mouth inflations of the lungs.

It is admitted that estimates of the amount of blood lost in labor are likely to be inexact, but nevertheless will serve to compare the incidence of postpartum hemorrhage. Assuming an estimate of 500 c.c. or more of blood as a postpartum hemorrhage, this degree of hemorrhage was found in 6 per cent under our former routine as compared with 2.6 per cent under paraldehyde. The greater amount of rest during labor and the smaller amount of ether used may be factors in this improvement.

Spontaneous delivery occurred in 81.2 per cent as compared with 79 per cent under our former routine. The involuntary bearing down efforts are excellent in the majority of cases, but since they are probably not quite as efficient as the voluntary efforts of the patient who is awake, we have compensated for this to some extent by the intranasal administration of pituitary extract in 37 per cent, and the more frequent use of episiotomy under novocaine, to remove the resistance of the perineum during the latter stages of crowning.

Low forceps were used in 11 per cent and midforceps in 7.8 per cent under paraldehyde, as compared with 10 per cent and 8 per cent in our former routine.

It can be seen from this table, that all the major obstetric procedures can be handled with ease and with the conscious cooperation of the patient. The only procedure which we would not advise performing under epidural anesthesia is version and extraction. This might prove difficult because the uterine contractions continue unabated under the anesthesia, and for version one needs relaxation in order to accomplish it easily without danger to mother or child. This point was also brought out by M. P. Rucker⁴ in 1930.

TABLE III. POSITIONS AND PRESENTATIONS

O. L. A.	24
O. D. A.	5
O. D. P.	6
O. D. T.	4
L. S. P.	2
O. L. T.	2
O. L. P.	2
Not recorded	30
L. S. A.	1
	<hr/> 76

The positions and presentations of the deliveries are included so that the reader may see the variety of cases dealt with.

TABLE IV. CESAREAN SECTIONS (10)

Indications:	
1.	Central placenta previa (placenta covered $\frac{3}{4}$ of os).
2.	Contracted pelvis with x-ray evidence of fetopelvic disproportion.
3.	Generally contracted pelvis with x-ray evidence of fetopelvic disproportion.
4.	Flat pelvis with x-ray evidence of fetopelvic disproportion; maternal signs of exhaustion.
5.	Generally contracted pelvis (previous cesarean section done).
6.	Postmaturity, contracted pelvis with x-ray evidence of fetopelvic disproportion.
7.	Generally contracted pelvis with x-ray evidence of fetopelvic disproportion.
8.	Flat pelvis, fetopelvic disproportion, rheumatic heart disease (Sterilization and section).
9.	Generally contracted pelvis, previous cesarean section.
10.	Chart not available.

The procedure which we have followed in administering epidural anesthesia is that which Dr. Charles B. Odom² described in his recent article.

I should like to emphasize a point brought out by Odom that "the back should not be arched until all has been prepared prior to the introduction of the needle into the epidural space. The flexion of the back causes an inflow of blood into the peridural venous plexus which might dilate the veins and compensate in part for the increased negative pressure and at the same time increase the likelihood of venous puncture." We had some difficulty in visualizing the movement of the fluid in the indicator until we utilized this point and one brought forth by Bonniot,³ who observed

labors, coramine should be given to induce more prompt and thorough expansion of the lungs. The incidence of forceps delivery is not increased.

It has been a gratifying experience to note the confidence with which patients approach the time of labor, the refreshed state in which they react some hours after delivery, and the oft-repeated statement that the relief experienced had removed the dread of a future labor.

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EPIDURAL ANESTHESIA IN OBSTETRICS

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IN THE Charity Hospital of New Orleans, we have attempted to add to the anesthetic armamentarium of the obstetrician another procedure, epidural anesthesia, which we have thus far administered to 76 patients.

ANALYSIS OF CASES

TABLE I. OBSTETRIC CASES WITH EPIDURAL ANESTHESIA

AGES	11-20	20-30	30-40
No. of Cases	23	46	7
73			
White	31	Colored	45

The age group varied from our youngest patient eleven years of age to forty years, the majority of the cases falling in the age group between twenty and thirty years. There were 45 colored patients and 31 white patients to whom the anesthetic was given.

TABLE II. TYPES OF DELIVERY

Spontaneous	23 cases
Low forceps and episiotomy	24 cases
Midforceps	9 cases
Cesarean sections	10 cases
Versions and extractions	3 cases
Dührssen's	1 case
Embryotomy	1 case
Twins with Piper's forceps	1 case
Precipitation	1 case
Scanzoni and episiotomy	3 cases

ONSET OF ANESTHESIA

The onset of the anesthesia was observed to vary considerably after the injection of the anesthetic solution. In some cases the patients were given almost immediate relief and in others, twenty to thirty minutes elapsed before the patient was relieved of the pains of uterine contractions.

The uterine contractions were not interfered with in any of the cases. They continued unabated and often seemed increased in frequency and intensity. This was reported by M. P. Rucker who discussed the action of adrenalin as cause for delay in uterine contractions after the administration of the anesthetic. He no longer uses adrenalin unless especially indicated, and observed that the pains continued. The action of adrenalin on uterine contractions is also discussed by Bourne and Burns.⁷

TIME OF ADMINISTRATION OF ANESTHETIC

In administering the anesthesia, we have attempted to determine how soon the patient would deliver so that the anesthesia would not wear off before delivery occurred. We knew that the anesthesia lasted from one and one-half to two hours and attempted to judge the cases individually and according to the procedure anticipated in order to complete the delivery. We found in primiparae that, if we gave the injection when the cervix was almost completely dilated and the head was at station 0 to plus 1, the patient had a painless second stage of labor and that after delivery, we had time to repair episiotomies or lacerations, if they occurred, without any additional anesthesia. In multiparae, it was more difficult to determine the time to administer the anesthesia. We chose the time at which the patient was having strong, regular contractions and the cervix was 4 cm. or more dilated. In a few cases in which we misjudged the time of delivery, it was necessary to supplement the epidural anesthesia with nitrous oxide in order to terminate the labor.

We at no time saw asphyxia in the newly born infants which could be attributed to the use of the epidural anesthesia.

The third stage of labor is also benefited by this form of anesthesia in that the tonic of the uterus is not interfered with and blood loss is lessened.

RESULTS

TABLE VI. RESULTS

Good	68
Partially successful	5
Reactions	3

We have three patients who had a reaction to the anesthetic. One case was a mild reaction during which the patient had an excited facial expression, with increased respiration and pulse rate; she became pale

that the negative pressure in the epidural space changes with the change in the position of the patient. Bonniot states that when the patient is placed on an incline of 35 degrees the pressure passes from minus $\frac{1}{2}$ cm. to minus 5 cm. of water and when returned to horizontal the pressure returns again to zero.

We have been using the second lumbar interspace as a routine to enter the epidural space. Cleland's⁵ brilliant experimental and clinical studies show that the uterus is supplied by the eleventh and twelfth thoracic roots and the birth canal by certain undetermined sacral roots. In utilizing the second lumbar interspace, we are in close enough proximity to the eleventh and twelfth thoracic roots to obtain excellent anesthesia of these roots by diffusion of the anesthetic solution. This interspace is also advantageous in that the epidural space is larger in this region than higher up in the spinal canal (Odom, Houdard, Judet, Mathey¹¹) and the spinous processes of the vertebrae come off in a horizontal plane, whereas, higher up they come off in a more vertical plane, making for difficulty in the injection of the anesthesia (Giordanengo¹⁰).

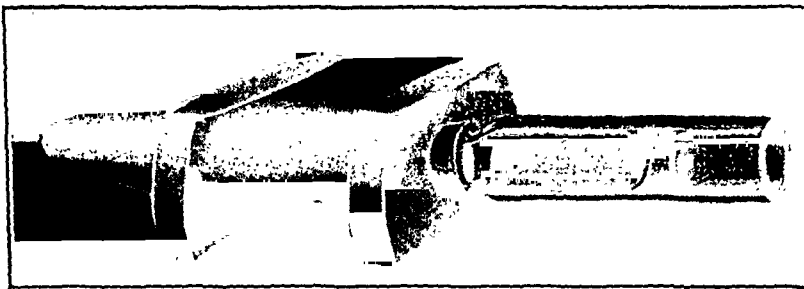


Fig. 1.—Spinal needle with glass indicator in place partially filled with water. Negative pressure in epidural space draws the water inward.

AMOUNT OF ANESTHESIA

The amount of anesthetic solution used has been changed from time to time in trying to find a solution in which the duration of the anesthesia was lengthened. The patients in the recent cases on our service (32) were given 500 mg. of novocaine and 2 ampules of 1 per cent Pantocain dissolved in 50 c.c. of sterile saline. This mixture gave an anesthesia lasting from one and one-half to two hours.

TABLE V. AMOUNT OF ANESTHETIC USED

500 mg. novocain	}	32 cases
2 ampules pantocain		
60 c.c. 1 % procaine		13 cases
50 c.c. 1 % procaine		2 cases
50 c.c. $\frac{1}{10}$ % pantocain		2 cases
50 c.c. $\frac{9}{10}$ % procaine	}	3 cases
1 % pantocain		
100 c.c. 1 % procaine		3 cases
Not recorded		21 cases

4. Although there are dangers in the administration of the anesthetic, care coupled with the negative pressure technique all but obviates them.

5. The uterine contractions are not interfered with after giving the anesthesia; there is no asphyxia in the newborn ascribable to the anesthetic; and blood loss is lessened in the third stage due to the tonicity of the uterus.

6. The reactions which occurred were probably due to either faulty technique or sensitivity to the anesthetic solution.

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A RÉSUMÉ OF ONE HUNDRED CONSECUTIVE CASES OF ECTOPIC PREGNANCY

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THIS study was made from the records of 100 consecutive cases of ectopic pregnancy treated in the Surgical Division of the City Hospital of Akron during the five-year period from 1931 to 1936.

In this series, the patients for the greater part were admitted late and therefore the Friedman test, necessitating a forty-eight-hour delay, was not considered a justifiable procedure. It might, however, have been of some value were it used in the early unruptured cases.

There were 95 white and 5 colored women ranging from eighteen to fifty years of age. Of these, 95 were married and 5 were single. In this hospital the ratio of black to white admission runs about 5 per cent. There were 22 patients who were eighteen to twenty-five years of age, 59 who were twenty-five to thirty-five, 18 whose ages fell between thirty-five and forty-five, and 1 past forty-six.

From the histories examined it was found that 28 patients had experienced 1 to 7 previous abortions. Of 38 patients, 14 had had 1 child; 17, 2; and 7, 3 or more. Three patients had had 1 stillbirth each, delivered at term. The above births were exclusive of two classical cesarean sections.

The occurrence of previous pelvic inflammation as regards history was evident in 21 patients. Of these, 6 gave histories of Neisserian infection, 3 had had "pus tubes," and 7 had experienced longer or shorter febrile periods postpartum. One patient, five years prior to her ectopic pregnancy, had undergone a vaginal hysterectomy on her second day postpartum because of complete inversion of the uterus.

Including the vaginal hysterectomy noted above, 12 patients had had previous abdominal operations. These are outlined in Table I.

and broke out in cold perspiration. We administered adrenalin and caffeine and she promptly was relieved and began feeling better. The second case occurred in one of our cesarean sections. After the anesthetic was administered the patient was prepared and draped. She then became excited, moved her lips as if trying to talk but was unable to utter a sound. She became very pale and passed into profound shock. The respirations ceased and artificial respiration was started. The pulse rate remained good for a short time but this too soon became imperceptible. The head was lowered, intravenous adrenalin (minims X) and seven and one-half gr. caffeine administered, and an infusion started. It was feared for a time that the patient had died. A quick cesarean section was performed in order to save the infant from asphyxiation and a normal child with spontaneous cry and respiration was delivered. After the delivery of the infant the patient slowly rallied, the pulse became bounding and rapid (probably from the effects of the adrenalin), and spontaneous respirations were resumed. The operation was completed as quickly as possible; acacia was started intravenously and external heat applied. The patient made an uneventful recovery and was discharged from the hospital in twelve days.

The third case with a reaction was a primipara who apparently received some of the procaine solution into the subarachnoid space, as she lost consciousness, and it was with difficulty that respiration and circulation were restored. Heroic doses of ephedrine and adrenalin and the use of the Drinker respirator were necessary to bring the patient back to consciousness. However, there were no deleterious effects manifested when the birth of the child with low forceps took place. The child cried lustily after it was born and both mother and child made uneventful recoveries.

The reactions which we had were attributed to two causes: Either, owing to some fault in the technique, the anesthetic was given into the subarachnoid space, or the patient had a sensitivity to the novocaine solution used. The operator must be extremely careful in administering the anesthetic to make sure that the anesthetic solution is entering the epidural space and that he has not traversed this space and is depositing the solution into the subarachnoid space.

CONCLUSIONS

1. This form of anesthesia should be part of the armamentarium of every experienced obstetrician and anesthetist.
2. The anesthetic can be administered to all patients in the child-bearing age.
3. All the major operative obstetric procedures can be performed under this form of anesthesia safely and with the conscious cooperation of the patient, except in version.

The patients gave histories of having been sick for from one to fifteen weeks. In Table III the periods of illness in weeks are given.

TABLE III. DURATION IN WEEKS OF ILLNESS PRIOR TO OPERATION

	CASES
Less than 1 week	18
1 to 2 weeks	28
2 to 3 weeks	12
3 to 4 weeks	17
More than 4 weeks	22
No record	3

Sixteen patients remained in the hospital from two to six days before operation. Of these, only 4 including the abdominal pregnancy were suspected of having an ectopic pregnancy according to the records. The patient with the abdominal ectopic pregnancy remained in the hospital under observation for seven days prior to operation. The correct diagnosis was suspected when first seen. However, it became definite only after the patient suddenly went into shock. At operation a five months' fetus and placenta were removed without event. The abdomen contained about 2,000 c.c. of free blood. In the remaining 12, the preoperative diagnosis was as follows: 3 acute or chronic salpingitis, 2 acute appendicitis, 3 twisted ovarian cysts, 1 ovarian cyst, and 3 infected incomplete abortions.

The preoperative leucocyte count, differential and the hemoglobin determination were noted in 89 cases and their ranges are given in Table IV.

TABLE IV

WHITE BLOOD COUNT	CASES	POLYNUCLEAR LEUCOCYTES	CASES	HEMOGLOBIN (SAHLI)	CASES
Less 10,000	29	Less 70%	22	Less than 50%	26
10,000 to 15,000	26	70% to 75%	30	50% to 70%	39
15,000 or more	34	75% to 80%	20	70% to 100%	24
No record	11	80% or more	17	No record	11
		No record	11		

Shock was evident in 28 of the patients admitted. This diagnosis was made on the basis of subnormal temperature, pallor, thready pulse, and low blood pressure. Of the 28 in shock, 26 were correctly diagnosed as ruptured ectopic tubal pregnancy. The remaining 2 were diagnosed as ruptured peptic ulcer in one case and ruptured ovarian cyst in the other. This is excusable since the one patient diagnosed as ruptured peptic ulcer had given no history referable to the pelvis, but did give a long history of ulcer distress. The case diagnosed as ruptured ovarian cyst was seen for the first time in the Outpatient Department and gave no history of amenorrhea, subsequent bleeding, or pelvic pain. She had been told by a doctor in the past that an ovarian cyst was present.

Pelvic examination was recorded in 90 cases and the more important findings noted in Table V.

TABLE V. FINDINGS ON PELVIC EXAMINATION IN ECTOPIC PREGNANCIES

VAGINAL BLEEDING	SLIGHT UTERINE ENLARGEMENT	PAIN ON MOTION OF CERVIX	ADNEXAL MASS	BULGING OF CULDESAC
62	57	85	89	67

In one instance only was Cullen's sign (discoloration around umbilicus) noted and that was in a patient who had had a previous classical cesarean section

TABLE I. PREVIOUS OPERATIONS

CASES	OPERATION	YEARS BEFORE ECTOPIC PREGNANCY	DIAGNOSIS
3	Appendectomy	3, 7, 2	Acute appendicitis
3	Salpingo-oophorectomy 2 right, 1 left	3, 2, 6	Ectopic tubal pregnancies
1	Vaginal hysterectomy	5	Postpartum eversion of uterus
2	Classical cesarean section	6, 10	Placenta previae, disproportions
3	History of previous pelvic laparotomy	3, 7, 4	Pus tubes

As regards relative sterility there were 32 patients who had not conceived in a period of five years or longer prior to the ectopic pregnancy. This is in keeping with the previously published reports found in the recent literature.

Of the 100 cases herein reported, 31 patients gave a history of 1 to 3 attacks of fainting. Twenty-seven gave histories of weakness or dizziness and in 20 patients fainting was denied. There was no reference to these symptoms in the remaining 22 histories.

Pain was the most common subjective symptom: it occurred in 95 cases, 56 times on the right side and 39 times on the left side. It is interesting to note here that there were 55 right and 42 left ectopic pregnancies. The character of pain complained of was described as being "knife-like" in 43 cases. Since there were 78 cases of rupture it follows that tearing of the peritoneal coat does not, in every instance, account for the sudden "knife-like" pain. "Sticking" pain was commonly complained of and more often in the unruptured cases. Three patients gave histories of severe right shoulder pain.

Amenorrhea was the next most common symptom: 62 patients had missed 1 or more periods. In this classification 34 patients had not missed any period. However, upon closer questioning they either menstruated earlier or later than the expected date. Bleeding or spotting after a more or less irregular menstrual period was a chief complaint. Seventy-four patients presented this complaint as noted in Table II.

TABLE II. PERIODS MISSED AND NUMBER OF DAYS OF BLEEDING OR SPOTTING

PERIODS MISSED	CASES	NO. OF DAYS OF BLEEDING OR SPOTTING AFTER AN IRREGULAR MENSTRUAL PERIOD	CASES
0	34	No bleeding	22
1	34	1 to 10 days	22
2	19	10 to 15 days	17
3 or more	9	15 to 25 days	10
No record	4	25 or more	25
		No record	4

The spotting was rather irregular since as many as 5 days would elapse during which time there was no bleeding or staining. In 23 cases patients gave a history of having passed "clots." In no instance were these examined, either grossly or microscopically. If the patients could be instructed to save these "clots" or shreds of tissue, a histologic examination would in many instances reveal the correct diagnosis. It is known that a decidual reaction is produced in the uterus, even if the pregnancy occurs outside this cavity and chorionic villi are found only where the products of conception are implanted.

Pelvic examination: There was a right adnexal mass the size of an orange which was extremely tender and seemed to be attached to the uterus. Motion of the cervix caused pain. Blood pressure, respiration, pulse, and temperature were all normal. Hemoglobin was 11.1 gm./100 c.c., R.B.C. 3.9 million, W.B.C. 13,400. Patient remained in the hospital for six days, after which time a surgeon was consulted and decided to operate for "right pelvic mass." Operation revealed unruptured right ectopic pregnancy. The sac was incised, fetus removed, and the sac packed with gauze. Sutures were placed through the sac and broad ligament and the abdomen was closed, leaving a drain tube in place. One hour after operation the patient was given 400 c.c. of whole blood and 1,600 c.c. of saline intravenously. She died two hours later, supposedly of hemorrhage. No autopsy was performed.

CASE 69321.—Patient, white, aged twenty-four years, para ii, gravida iii, considered herself three months pregnant. Her last period occurred three months before admission. She gave a history of having had crampy pains in the left lower abdomen for past week. About twenty-four hours prior to admission, while straining at stool, she had a severe knifelike left lower abdominal pain that caused her to faint. Patient was first seen the next morning when she was sent to the hospital. She appeared acutely ill. Her blood pressure was 70/50, and pulse 130. The abdomen was dull in both flanks and markedly distended. Immediate operation was done, and a ruptured left tube and a three months' intact fetus were found free in the abdomen. Left salpingo-oophorectomy was completed. About 4,000 c.c. of fresh blood were aspirated aseptically and were autotransfused into the patient's basilic vein. Her condition remained poor, and she died four hours postoperatively in profound shock. No autopsy was performed.

CASE 50723.—Patient, white, aged twenty-three, para ii, gravida iii, had her last period nine weeks previously. There had been spotting almost continuously for this period, and for the last five weeks there was intermittent colicky pain in the left side of the abdomen. The night prior to admission, while hanging curtains, patient had a severe left lower quadrant knifelike pain which caused her to faint. She remained in bed until next morning when she was admitted to the hospital. Pelvic examination revealed a left adnexal mass, the size of an orange, and a distended cul-de-sac of Douglas. Preoperative laboratory work revealed 13.9 gm. Hb, 4.1 R.B.C., 12,600 W.B.C., with 71 per cent polymorphonuclears. Patient immediately was laparotomized and a ruptured left ectopic pregnancy was found. There was about 1,000 c.c. of fresh and clotted blood free in the abdomen. We did a left salpingo-oophorectomy and a right salpingectomy. No transfusions were given. The patient died twelve hours postoperatively, very suddenly, and the cause of death, revealed by autopsy, was bilateral atelectasis. Both lung bases were filled with antemortem thrombi.

CASE 50797.—Patient, white, nullipara, aged twenty-eight years, had always had normal menses until five weeks previously, at which time she began to menstruate and has continued to spot and bleed ever since. She had had "sticky" pains in right lower abdomen for past ten days; however, these had never been severe. The patient did not appear acutely ill. She had direct and rebound tenderness in the right lower quadrant, supposedly over McBurney's point. Hemoglobin was 80 per cent, W.B.C. 11,300, with 82 per cent polymorphonuclears, and the urine was negative. Preoperative diagnosis was chronic appendicitis with uterine hemorrhage. At operation a ruptured left tube with about 100 c.c. of free and clotted blood in the abdominal cavity was found. The ectopic pregnancy was in the ampullar end of the tube and appeared as an ectopic abortion in progress. The surgeon did a left salpingectomy, appendectomy, and cholecystectomy (for gallstones). The operation took one hour and fifteen minutes. The patient had a very stormy course and died on the sixth day of generalized peritonitis. No autopsy.

As a preoperative measure cul-de-sac puncture was recorded 4 times. In each instance fresh or clotted blood was aspirated and the patient was submitted to immediate laparotomy.

Bush⁵ presented 161 cases in 1934 of which 46 had diagnostic puncture. He advised that this procedure be used more frequently, and also suggests using a large caliber needle so that small blood clots would not obstruct the lumen and give a false test. This author points out a possible fallacy of the test in that ruptured corpus hemorrhagica will frequently produce copious intra-abdominal hemorrhage. Greenhill⁶ reports three of his own cases and in addition collected 77 others from the literature where abdominal hemorrhage was produced by corpus hemorrhagica rupture.

Twelve patients had dilatation and curettage prior to laparotomy as a diagnostic procedure. The finding of normal or hypertrophic endometrium in a patient whose symptoms and signs suggested ectopic pregnancy or threatened abortion is a diagnostic aid in favor of the former.

Colpotomy was done in 4 instances. These patients were operated upon early in the five-year period. "T" tubes were inserted and immediate laparotomy instituted. All of these patients except one had long hectic postoperative recoveries.

Of this series there was a correct diagnosis in 80. This percentage of correct diagnosis is in keeping with those recently reported by James and Lafferty,⁷ Meagher,⁸ and Folk and Rosenbloom.⁹

TABLE VI. POSITION OF RUPTURED AND UNRUPTURED ECTOPIC PREGNANCIES FOUND AT OPERATION

Ruptured right	43
Ruptured left	35
Unruptured right	12
Unruptured left	7
Ruptured abdominal pregnancy with hemorrhage	1
Not stated	2

Of the 100 cases investigated, 78 patients presented ruptured ectopic tubal pregnancies. At operation large quantities of free and clotted blood were found in the abdomens of 68 and an estimate of more than 200 c.c. in the remaining 10.

The 100 operations were done by fifteen different operators. In three cases during the early period of this series, drains were inserted after the bleeding structure was removed. From the records there was no evidence of acute inflammatory condition necessitating drainage mentioned. However, these early records were not always complete. These patients in the drainage cases did poorly and one died.

FATALITIES

CASE 45210.—Patient, white, aged thirty-two years, para iii, gravida iv, last baby seven months old, gave a history of miscarriage five months ago but was not attended by a physician. She had had slight vaginal bleeding and right abdominal pains for past six days. The menses had not become established since last pregnancy. For past three days there had been nausea and vomiting, and pains in the lower abdomen for the past two days had been sharp and intermittent. She was an obese white female of stated age who did not appear acutely ill.

SUMMARY AND CONCLUSIONS

1. Ectopic pregnancy occurred in the City Hospital of Akron 100 times in the five-year period from 1931 to 1936.
2. Fainting, dizziness, or weakness was recorded 58 times; in 11 these symptoms were not mentioned.
3. Missed or delayed periods usually with subsequent spotting occurred 74 times.
4. Pain, either "knifelike" or "sticky," was complained of in 90 patients.
5. Of the 90 pelvic examinations recorded 89 presented adnexal masses which proved to be ectopic tubal pregnancies at operation.
6. Cul-de-sac puncture as a diagnostic method was done 4 times. Colpotomy with "T" tube drainage was instituted twice with adverse results.
7. The white, differential blood count, and hemoglobin determination were given in 89 cases.
8. The Friedman test was used infrequently.
9. Whole blood transfusions were used 12 times and the average amount was 500 c.c. Autotransfusion was used 22 times with an average of 1,700 c.c. in each instance.
10. One hundred patients were operated upon with a mortality rate of 5 per cent and the causes of death are given.
11. Early diagnosis and conservative operations are urged. In 43 cases the ovary was removed along with the affected tube. This number of extirpated ovaries is considered unnecessarily high.
12. Abdominal drainage was used in 3 cases. The reason was not given.
13. Unwarranted additional surgery apparently contributed to the mortality.
14. Abstracts of the case histories of the 5 patients who died are presented.
15. The average postoperative stay in the hospital in the group which recovered was found to be slightly greater than nine days.

I wish to express my appreciation to Dr. Charles C. Pinkerton for many valuable suggestions in the preparation of this report and also to thank the Surgical Staff of the City Hospital of Akron for their permission to publish the cases herein reported.

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CASE 70738.—Patient, white, aged twenty-three years, no previous pregnancies in her four years of married life. Her last period was in September. However, she began to bleed in October and continued to spot and have intermittent profuse vaginal bleeding to date. About ten days prior to admission the patient had a rather severe right lower abdominal "colicky" pain. She was observed for five days at home by her family doctor without a definite diagnosis. She was pale, appearing acutely ill. Her blood pressure was 80/50, pulse 150, and temperature 101.8° F. The abdomen was distended, very tender in the right lower quadrant, and there was definite dullness in both flanks. Pelvic examination: Right adnexal mass size of an orange appearing in cul-de-sac of Douglas which was pushed forward. Diagnosis: ruptured ectopic tubal pregnancy. Hemoglobin was 50 per cent, W.B.C. 17,800, with 85 per cent polymorphonuclears, and the urine was negative. Operation under ether anesthesia revealed right ruptured tubal pregnancy. After doing a right salpingectomy, 3,000 c.c. of aspirated blood were transfused and there were 4,500 c.c. of fresh and clotted blood in the cavity. The fetus was intact in the "sac," and it appeared of about two months' size. The patient began coughing on the first day and died on the third with a diagnosis of right lobar pneumonia. No autopsy was performed.

From Table VII it will be seen that in addition to the removal of the bleeding ruptured tube, 43 ovaries were extirpated. It is clear that removal of the ruptured salpinx alone is not always feasible. Occasionally the ovary is so agglutinated to the ruptured tube that separation without the risk of increased hemorrhage or of subsequent bleeding is not considered possible. It would seem, however, that greater conservatism could have been practiced in this series. Unnecessary extirpation of the ovarian tissue in such a group may be of serious moment. However, great care in the matter of conservatism was also evident on the part of several of the operating surgeons. Additional surgery such as appendectomy, hysterectomy, uterine suspension and cholecystectomy is, of course, unwarranted. In 2 of the 5 patients who died additional surgery was evidently a contributing factor.

TABLE VII. STRUCTURES REMOVED AT OPERATION

Bilateral salpingectomy and oophorectomy	14
Unilateral salpingectomy and oophorectomy	43
Salpingectomy	42
Appendix along with primary operative procedure	22
Hysterectomy along with primary operative procedure	4
Suspension along with primary operative procedure	2
Cholecystectomy along with primary operative procedure	1
Gauze pack of affected tube	1

Transfusion of whole blood was used 12 times and autotransfusion given 22 times. The average amount of whole blood given was 500 c.c. and the average amount of autotransfusion was 1,700 c.c. The greatest amount of blood aspirated from the abdomen and replaced into the general circulation was 3,700 c.c. This method of replacing blood lost has proved very effective in this institution and is to be highly recommended. The free blood is aseptically siphoned into a flask containing 25 c.c. of 5 per cent sodium citrate to each 500 c.c. of blood and immediately inserted usually into the basilic vein by gravitation. There have been no demonstrable ill-effects to date from the autotransfusions given.

The postoperative convalescence was satisfactory in all the recovery cases except those submitted to posterior colpotomy with "T" tube drainage, and those submitted to postoperative abdominal drainage.

sure nor albuminuria, but there was definite tenderness of the fundus uteri. The blood serum remained definitely antiproteolytic. As there had been no improvement on the oil therapy, an inquiry was made as to the preservation of the batch which was being used. We found that the patient had been given the dregs of a Winchester of the oil received in June, 1935, which, however, was not noticeably rancid. A new supply of the oil was prepared and given until term by the same routine as before. There was a prompt subsidence of hemorrhage, uterine and low back pains, fundus tenderness. When an opportunity to test the blood again presented itself on October 10, the serum had reverted to normal. It remained so on occasional tests until the delivery at term of a normal female child weighing six pounds seven ounces.

Another patient was given the same wheat germ oil sample as had been used in the last case described, because of symptoms and signs of a threatened premature delivery, on June 25, 1935. All her symptoms were controlled and her blood serum reconverted to normal digestibility until July 20. When next seen, on August 8, her previously normal blood pressure had risen to 142/84, fundus tenderness and albuminuria had developed. At the time of delivery of a normal eight-pound male child on August 18, her serum had again become antiproteolytic, although she had taken her oil faithfully in a dosage which had proved adequate until August. We have done over 2,400 tests on blood sera for the antiproteolytic estrogenic factor and have never yet found a patient's blood serum antiproteolytic after she had received an adequate dose of a fresh preparation of a potent wheat germ oil.

Four patients, of whom one had had one previous spontaneous abortion, and another two previous miscarriages, but none of whom had borne living children, were almost simultaneously put upon wheat germ oil capsule therapy in the early part of November, 1935. The oil used had been prepared on Oct. 21, 1935. Simultaneously about Christmas time all four patients began to exhibit evidences of escape from the influence of the oil. The blood of three of the four had become antiproteolytic for the first time since therapy had been begun. The blood of the fourth could not be secured for testing. One patient developed a Couvelaire apoplexy of the lower segment of the uterus. Enormous doses (30 per day) of the same wheat germ oil capsules that she had been using for months could not control her uterine tenderness and rigidity, nor render her blood normally digestible, and a cesarean section was finally performed after doses of fresh bulk oil had accomplished with their accustomed promptness all the old capsules had failed to do. The diagnosis of uterine apoplexy was strikingly confirmed at operation. Fortunately, the child survived its difficult experience. Another of these patients suddenly developed continuous uterine pain and fundus tenderness, bled from the uterus, and her blood simultaneously became antiproteolytic. Fresh bulk oil corrected all this promptly, as usual. The third patient had twice miscarried at six and a half months and at this Christmas season was only three months pregnant. She developed no evidences of abortion, but a general malaise and some attacks of dizziness. Her blood had also become antiproteolytic. Fresh bulk wheat germ oil promptly rendered her blood serum normally digestible and corrected her symptoms. By means of the continued use of fresh bulk oil, regularly checked by blood tests for the recurrence of the antiproteolytic factor in the blood, she went to term and delivered a normal baby. As she was a marked hypothyroid, however, she required as much as six drams of the oil each day toward term. The symptoms of the fourth patient, uterine tenderness and sudden gain of seven pounds of weight (her blood could not be tested), were also promptly corrected by the administration of fresh bulk wheat germ oil.

Unfortunately we have had no opportunities to check these observations on the preservation of potency of wheat germ oil on rats. What

WHEAT GERM OIL THERAPY

II. PRESERVATION OF POTENCY, INFLUENCE ON LABOR, SEASONAL NEEDS

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PRESERVATION OF POTENCY

WHAT are the conditions which govern the preservation of potency of a wheat germ oil preparation? Is potency retained more effectively in bulk or in capsule form? Have extremes of temperature any influence on it, and if so, what? Gradually some opportunities have presented themselves by which an estimate of these factors has been reached.

Not infrequently patients both in the clinic and in private practice had their complaints controlled by means of wheat germ oil. That is to say, their symptoms and signs of threatened abortion or threatened abruptio placentae, for example, had disappeared. When next seen these patients sometimes displayed the same symptoms and signs for which the wheat germ oil had been administered, although they had followed directions carefully and taken their oil regularly in what had hitherto proved to be an adequate dosage. This was noticed by us especially during the winter months, and on inquiry we usually found that these women had neglected to keep the oil cold. They had left the oil at room temperature for days, in rooms which were often very warm. When fresh samples of the oil were given to them, the original regime proved quite as effective as at first, and they were promptly and permanently brought under control again. Accordingly we warn every patient nowadays to keep her oil in the refrigerator or some other cool place, and, indeed, insist that local druggists adopt the same precautions. All this in spite of Evans¹ original observation on the resistance of vitamin E to high degrees of heat.

The case histories of a few patients will illustrate the duration of the potency of oil kept under optimal conditions.

A patient whose first pregnancy had ended in a stillbirth due to abruptio placentae, came under observation at the fourth month of her second pregnancy. The last menstruation had begun on May 18, 1935. On June 15, she first noticed some edema of the extremities. On September 14, a severe low backache began and continued for seven days. At the same time some intermittent uterine cramps were felt and she felt nauseated and miserable. On September 17, her blood serum was anti-proteolytic² and she was given wheat germ oil in bulk, four drams at each dose three times within the first twenty-four hours, then one dram each day. On September 18, there were intermittent low back pains for several hours. On September 21 and 23, there were small uterine hemorrhages of bright red blood, accompanied by intermittent back pains and uterine contractions. There was no elevation of blood pres-

Moreover, many women were tested just after or during normal parturition at term by our blood test for the antiproteolytic factor described by us. No more than the usual 10 per cent² of these normals displayed the presence of such an estrogenic^{5, 6} factor in their sera. This observation, of course, seems difficult to reconcile with the observations made on increased urinary estrin output just before labor by Marrian and his coworkers.⁷ However, blood estrin and urinary estrin values may differ very greatly.⁸⁻¹⁰ Moreover, the Smiths¹² have very recently indicated that before the onset of labor or during labor in normal women, serum estrin may show no increase or even may fall. They also show that the level reached in these normal sera at labor does not exceed 1 rat unit per c.c. of serum, whereas our test for estrogenic substance will not disclose a content of less than 2.5 rat units per c.c. of serum.

It would appear, therefore, that the onset of labor at term is determined by several factors, of which the presence of an increase of blood estrogenic substance is only one, and by no means an essential nor invariable prerequisite. As vitamin E appears to act principally by neutralizing any excess of estrogenic substance in the bodily economy, there would a priori be no obvious reason why it should interfere with the onset or course of labor at term, and it does not do so. There is undoubtedly much more involved in the physiologic onset of labor at term than just the balance between vitamin E and estrogenic substance in the body.

In March, 1937, a patient two months pregnant was seen who had no evidence of impending abortion. A blood serum tested routinely revealed no excess of estrogenic antiproteolytic substance. However, three days later a spontaneous abortion began and proceeded slowly to its termination quite unaffected, as far as could be seen, by the administration of 12 drams of wheat germ oil, known to be potent, which were given each day for six days. We took this to be one of the small percentage of cases of spontaneous abortion not due to vitamin E deficiency, and therefore not affected by wheat germ oil therapy. Its interest in this discussion is that it indicates that wheat germ oil has no influence in stopping labor, even long before term, where that labor is not induced by a deficiency of E and concomitant excess of blood estrogenic substance. The decidua came away intact, and suggested very definitely that it had been located as a central placenta previa.

SEASONAL NEEDS IN WHEAT GERM OIL THERAPY

It is obvious that there should be a good deal more available vitamin E in the green diets of summer and early autumn in this latitude and country. For four consecutive years during the progress of this study, we have observed a very definite seasonal rhythm in the incidence of premature interruption of pregnancy, and in abruptio placentae and the conception of deformed fetuses in particular. All of these phenomena appear to have some relation to deficiency of vitamin E in our experi-

conclusions we have reached are based entirely upon purely clinical work. However, on the basis of experience with the cases described in detail above, and many more recent cases, we have come to believe that wheat germ oil, whether in bulk or in capsules, retains reliable potency very little longer than eight weeks. Indeed, if kept at room temperature we believe its potency may be lost in a very few days. We have made no effort to find preservatives for the oil.*

We hope that other workers will investigate this important question of the preservation of potency in more detail, with animals. Until the point is settled, many preparations of wheat germ oil being marketed must lie under some degree of suspicion.

INFLUENCE ON LABOR

Many of our patients who took wheat germ oil throughout the greater part of their pregnancies were so much impressed by its ability to prevent the premature occurrence of labor, that they hesitated to use it at or near term. They feared it would carry them beyond term. However, there appears to be no basis for such apprehension. It has been the author's practice to insist upon the use of the oil up to the very onset of spontaneous labor, because he feared the late development of abruptio placentae^{3, 4} if it were stopped prematurely. He has never observed that the onset of labor was unduly delayed in this way in the 60 cases in which it has been used continuously until labor began.

Moreover, we have repeatedly seen threatened or partial abruptio placentae occur at or near term in women who have never received wheat germ oil. In these cases we have felt that a preliminary preparation of the patient with oil before the indicated induction of labor would be helpful. When this was carried out, by the use of the usual massive dose of 12 drams of wheat germ oil given one day before the medical induction, the induction has been as successful as could have been expected had no oil been given, and the labor has proceeded as usual.

To demonstrate this even more clearly, we have recently attempted to stop labor early in the first stage in a small number of cases by means of the usual massive dose of wheat germ oil. Some of these patients were nauseated, as could be anticipated, and found our procedure very trying. However, in no case of the 10 cases attempted, did we detect any tendency for the labor to stop or be prolonged unduly.

*Recently Palmer (Industrial and Engineering Chemistry 9: 427, 1937) has reported rat assays on oil sealed in vacuo and kept cold for months. The residual potency displayed wide variations, but most of the samples were quite active for at least eight months. I believe, however, that a more sensitive test of E potency than the classical rat assay is the clinical response of a very common type of pregnant human patient, one having an incipient toxemia of the kind which frequently terminates in premature placental detachment. Most of these women have enough E to carry the fetus to term, but they do not have enough to prevent the appearance of toxemia of this particular sort. Wheat germ oil suitable for use in human pregnancy should do more than preserve pregnancy in the rat or in the human being; it should protect the latter from this toxemia.

3. The administration of wheat germ oil up to term does not delay the onset of labor nor prolong the duration of labor.

4. Green foods, such as lettuce and water cress, do not replace wheat germ oil in the treatment of the pregnancy complications related to deficiency of vitamin E in the human being. Milk may be an important factor in the diet as concerns its content of vitamin E.

5. Human males show a seasonal variation in the estrogenic substance in their blood, and hence in their assimilated vitamin E. This may have some bearing on male sterility.

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DIETARY HABITS DURING PREGNANCY*

WITH SPECIAL REFERENCE TO THE VALUE OF QUALITATIVE FOOD RECORDS

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FOR a number of years we have been using two different methods for determining or estimating the ingestion levels of various food elements of our research subjects. The methods were employed as a part of our study of pregnant women and the factors which might influence the growth and development of the human fetus. Since one of these methods consisted of the quantitative analysis of food aliquots, and the other of estimates based on qualitative records, and since the two methods were, in a number of instances, applied to the same patients, we have an opportunity to test the usefulness of the "qualitative" method by comparing its results with those obtained with conventional quantitative chemical analyses.

Because nutrition is one factor which influences vitally the status of both mother and child, we wished to extend the scope of our study to include a greater number of our subjects than could be included by

*Data for this paper have been collected at the Fels Research Institute by Miss Idell Pyle, Dr. Amy Hunter, Dr. Geneva Shong, and Miss Martha Potgieter.

ence. All of these pathologic conditions appeared more frequently from January to June each year and more infrequently from July to December.

Moreover, it has been our annual experience that larger doses of wheat germ oil were required by women with precarious pregnancies in the months from January to June each year. In many instances the dose was tripled. In our experiments on rats it has taken us from two to four months, and usually the latter, to render the animals sufficiently defective in vitamin E to cause spontaneous resorption of their fetuses. If the E deficiency in the diet were less marked we would have an approximate analogy to the observations we have made on human females. For the latter from November onward eat progressively less green food and drink milk whose origin is further and further removed from green fodder. These women, if pregnant, begin to display from February until June an increasing tendency to terminate their pregnancies prematurely.

Moreover, as would be expected, human males are not exempted from the seasonal tides of available vitamin E.

The author tested a number of unselected normal male medical students in the months of April and May, and also in the months of October and November, during 1936. It was found that 70 per cent of 36 such males tested in April and May revealed excess of estrogenic antiproteolytic substance in their blood sera. But in October and November only 50 per cent of 28 such males gave the corresponding result. That this last figure is so high is due, perhaps, to the very arid summer of 1936 and the resulting poor quality of green food available to these men in the months just prior to the time of testing their sera. These results may be compared with those of Frank and Goldberger,¹³ presumably secured not long prior to March, 1928, in New York City. They found that 7 or 15 per cent of 47 males whom they assayed gave a positive test for the presence of estrin in the blood by their biologic assay method. We have illustrated the inverse relationship of vitamin E and estrogenic substance in the body elsewhere.¹⁴

What importance such an observation has for the problem of male sterility remains to be seen. It has been shown¹ that male rats rendered deficient in vitamin E develop a testicular degeneration, which is probably irreversible, and that after five months sterility ensues.¹⁵ Moench¹⁶ has recently mentioned the use of vitamin E as a curative measure for sterility in the human male. One case of male impotence with gross testis atrophy which the author has seen has had return to potency and marked testis growth on vitamin E therapy.

SUMMARY

1. Wheat germ oil should be kept cold to prevent deterioration.
2. Wheat germ oil, in bulk or in capsules, retains reliable potency very little longer than eight weeks, even when so kept.

between-meal lunching. This type of record was kept for each day except in those instances in which travel, illness, or other emergency made record-keeping inconvenient. The subjects were impressed with the fact that we wished to have records filled out day by day. If, in any instance, this could not be done on the same day the food was eaten the record was to be skipped with the attitude that no feeling of guilt should result from the failure to record the day's menu.

When the records were complete the diets were tabulated. For this purpose a list was prepared on which all foods that had been eaten were classified into groups. These groups appear on Fig. 1 and in Table I. We went through the diet for each day, counted the number of times foods of each group appeared on the menu and recorded the

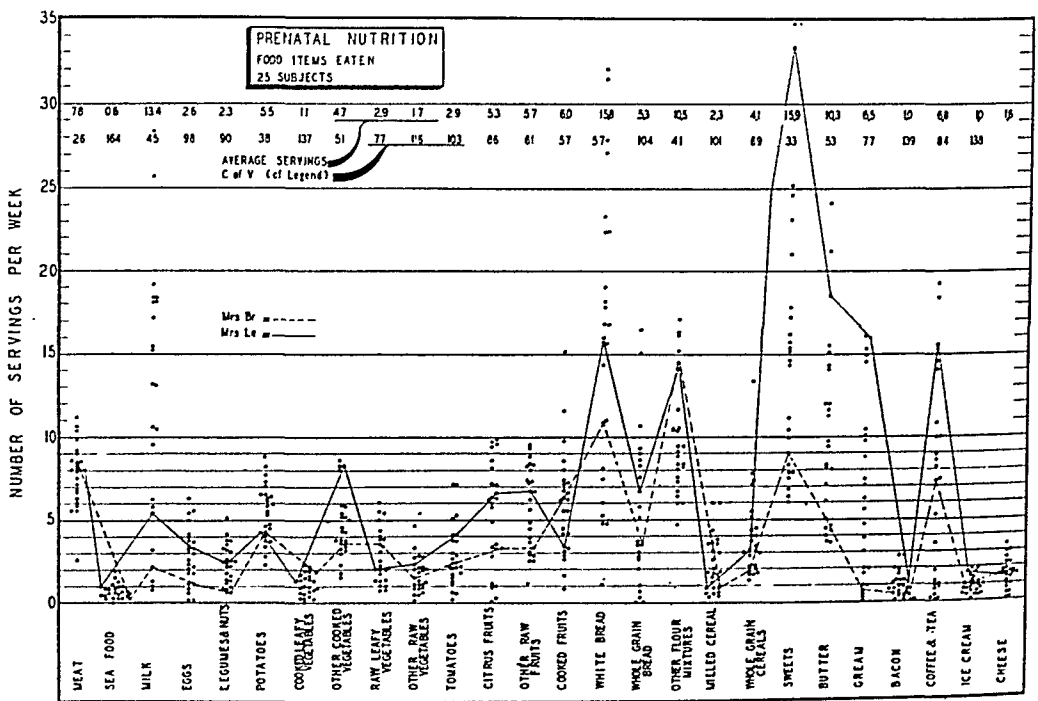


Fig. 1.—The points on the figure represent the number of servings per week for the several food groups which are indicated on the lower part of the figure. The scores for Mrs. Br. and Mrs. Le. have been followed through. The numbers in the upper quartile of the figure give the averages for the 25 women, and the average (25 women) for the coefficient of variation for the average number of servings per week. These coefficients indicate the extent of variation from one week to another.

number in the proper space of a tabulation sheet on which there was mimeographed a list of the food groups and spaces for recording the daily use, by number of servings, of these foods. When there was doubt as to which food group an item belonged, an extensive list, which had been prepared previously, served as authority.

The total period over which the diet was kept was divided into seven-day weeks starting at the delivery week and working back. For weeks having not more than two days missing, a seven-day total was computed on the basis of figures available. When more than two days were missing, the entire week was omitted. Next the weekly average

actual chemical work. We have attempted in this study to determine the value, if any, and the limitations of, a qualitative nutrition method as it was applied to our research material. Some of the dietary habits of 25 pregnant women of moderate to meager means are also considered in this paper. Their husbands were employed as follows: 8 engaged in small business, 7 college teachers, 4 farmers, 1 laborer, and 5 were not married.

RECORDING AND ANALYSIS OF QUALITATIVE FOOD DATA

In the "qualitative" method used, the patients were given mimeographed sheets on which there were spaces for recording each of the three meals of the day by items, the estimated quantities of some, but in most instances the number of servings. Thus for breakfast a mother might make a record something like the following: orange juice, $\frac{1}{2}$ glass; oatmeal, 1 serving with cream and sugar; white bread toast, 1 slice with butter; coffee, 1 cup with cream and sugar. Lunch and dinner would be recorded in a similar manner, as would also any

TABLE I. SIZE OF SERVINGS OBTAINED FROM QUANTITATIVE DATA

FOOD GROUP	AVERAGE SIZE OF SERVINGS OF FIFTEEN INDIVIDUALS*			AVERAGE BASED ON AVERAGE SERVINGS OF EACH OF THE FIFTEEN INDIVIDUALS	
	NUMBER OF SERVINGS	AVERAGE WEIGHT OF SERVINGS†	COEF- FICIENT OF VARIATION	WEIGHT OF SERVINGS	COEF- FICIENT OF VARIATION
Meat	111	68.9	44.8	71.3	26.6
Sea food	27	104.3	36.5	113.3	32.3
Milk	302	233.1	54.7	254.8	38.1
Ice cream	21	91.8	18.2		
Cheese	29	23.1			
Eggs	72	61.7	41.3	60.5	41.2
Legumes and nuts	40	82.1	66.3	91.5	53.8
Potatoes	70	93.4	53.7	95.0	33.5
Cooked leafy vegetables	21	116.8	45.0	116.3	27.7
Other cooked vegetables	53	67.2	64.0	65.2	69.4
Raw leafy vegetables	101	44.2	58.1	38.8	44.1
Other raw vegetables	48	48.9	61.1	39.5	40.7
Tomatoes	93	148.9	55.1	141.9	30.5
Citrus fruits	113	117.9	54.7	124.0	22.8
Other raw fruits	134	129.5	60.2	122.2	34.2
Cooked fruits	89	123.7	82.8	109.5	30.4
White bread	112	43.8	53.9	37.1	29.6
Whole grain bread	94	43.2	47.9	47.7	36.4
Other flour and meal mix- tures	112	44.3	77.6	38.3	71.0
Milled cereals	24	32.8			
Whole grain cereals	70	35.8	97.7	40.6	74.5
Sweets	227	20.8	96.3	17.9	53.2
Butter	232	13.9	72.4	13.8	34.1
Cream	83	63.0	68.2	62.5	24.0
Bacon	50	19.6			

*These 15 individuals include the 5 considered in Table II.

†Our data were adjusted to the figures in this column. The average was obtained by adding all of the serving weights and dividing by the number of servings. In column 4 an average was first obtained for each individual.

only (2) is free from obvious gross error as a result of the inaccuracy of attempting to classify food mixtures, the variability in the size of servings, and the variability in chemical composition of any given food. It is, of course, necessary to determine what error may be expected from these sources. To accomplish this objective we have compared the results of our qualitative determinations with quantitative determinations on the same subjects.

The chemical composition assigned to the food classes was based on the figures given in Waller's food table.* In the case of milk, ice cream, eggs, and other single items, the actual analysis, given as such, was used; but in such instances as cooked leafy vegetables an average was taken of the composition of a number of foods which are included in our classification of cooked leafy vegetables. In order to have a table with a uniform base for conversion purposes, a 100-gm. portion was chosen as the basic quantity.

The figures for the probable size of the serving were based on quantitative records of 15 women who have been used in balance studies in our laboratories. These records were analyzed and an average was taken of the actual weight of the servings. These average figures are given in Table II along with the number of weighings on which they are based and the coefficient of variation. As might be anticipated, the variation in size of serving was considerable. If, as we have done, the weight of the serving is computed from the group score as a whole and also from the 15 averages of the 15 individuals, there is good agreement between the two. The variation from one individual to another can also be seen from Table II.

TABLE II. COMPARISON OF QUANTITATIVE AND QUALITATIVE DIETS

SUBJECT	NUMBER OF OBSERVA- TIONS*	CALCIUM GM.	PHOSPHORUS GM.	PROTEIN GM.	FAT GM.
Mrs. L.	6	1.18 (1.50)†	1.57 (1.65)	79.0 (94.1)	106.1 (86.4)
Mrs. B.	7	1.21 (1.47)	1.50 (1.29)	70.5 (64.7)	94.3 (106.2)
Mrs. Pi.	8	1.01 (1.54)	1.29 (1.54)	67.7 (81.0)	87.8 (96.5)
Mrs. W.	3	1.22 (1.59)	1.38 (1.51)	68.1 (64.5)	none
Mrs. Pr.	6	1.82 (2.39)	2.16 (2.39)	110.0 (112.2)	none
The above com- bined	30	1.27 (1.69) $r = +0.70 \pm 0.06$	1.58 (1.67) $r = +0.73 \pm 0.06$	79.9 (83.7) $r = +0.80 \pm 0.04$	94.7 (94.7)‡ $r = +0.43 \pm 0.12$

*These observations were at approximately twenty-eight-day intervals.

†The figures in parentheses are those from actual quantitative analyses, some of which have been published elsewhere (Pyle and Huff).¹

‡Twenty-one cases.

With these figures available it is necessary to multiply the average number of servings of a food group per week by the average size of

*In order that there may be no misapprehension, it is pointed out that the qualitative method is adjusted to the records of 15 women; 5 of these are chosen for actual comparisons. If all 15 could have been used for actual comparison, the result would simply have amounted to a check on the figures for chemical composition of the food classes. In the present comparison, the 5 contribute to the estimate for the size of serving, and one would naturally expect that the size of their servings would be better adjusted than those of any random sample would be. This fact loses much of its significance when it is considered that the dilution, in every instance, is 1 in 15

number of servings of a food group was determined. The results of such tabulations are shown graphically in Fig. 1. Each point represents the average number of servings of a food group an individual had per week. It can be seen that the dietary habits of these 25 differed considerably, and when the scores for any particular individual are followed through, as has been done for two cases in Fig. 1, her peculiarities are at once revealed. Each point on Fig. 1 (a) varies with respect to the average of the entire group, and (b) represents an average of the several weekly scores; hence, a coefficient of variation can be computed for each point on Fig. 1.

The values for the average (average for the 25) number of servings of a given food item per week and the average of the above-mentioned coefficients of variation are given on Fig. 1. When all the women ate of a given food class frequently the group average was, of course, high; furthermore, if high averages are associated with low coefficients of variation and low averages with high coefficients of variation, a high group average indicates stability of ingestion of that item and vice versa. The actual correlation between the two items (group average of average number of servings per week and group average of the coefficients of variation of the individual average number of servings per week) was found to be -0.76 ± 0.06 . This gives a coefficient of determination (r^2) equal to 57.8. Hence, 57.8 per cent of the variation in choice of items from one week to another is associated with the number of times that item is eaten. This fact, we believe, has some bearing on the question of changes in diets during pregnancy; because the intake of food items which are taken frequently enough to be important in the nutrition of the patient also tends to remain stable throughout pregnancy.

ESTIMATING THE CHEMICAL COMPOSITION OF THE DIET FROM QUALITATIVE FOOD RECORDS

We have compared the results obtained from an analysis of the qualitative and quantitative data in order to show (1) within what limits quantity of ingestion of a given food element can be estimated from the qualitative records, and (2) whether the estimated quantities obtained from the qualitative records bear a fairly constant relationship to the actual ingestion, and, therefore, can be used for the relative rating of individuals.

In order to transform qualitative food records into estimates of the quantities of food elements, it is necessary (1) to group foods according to the likeness of their chemical composition, (2) to determine the average number of servings per time unit in each of these groups, (3) to determine what quantity of each food group most nearly represents the size of each serving, and (4) to employ tables of the average chemical composition of the various food groups. Of these procedures,

phosphorus of the other individual (Mrs. Le.) is also quite apparent. Her intake of meat, eggs, legumes, and nuts is almost average while her milk intake is low. Although there is considerable variation in size of servings, it is our feeling that the existence of a poorly-balanced or well-balanced diet shows up readily in Fig. 1. An actual comparison of qualitative and quantitative scores makes a more complete appraisal possible.

Of the 15 women from whose records Table I was constructed, 5 had qualitative records and at the same time had cooperated in a number of balance studies which have been described by Pyle and Huff.¹ It was, therefore, possible to compare the actual food analyses on the metabolism days with the qualitative estimates for those same days.² A summary of such a comparison is given in Table II. There is fair agreement between the quantitative values and the qualitative scores. The calcium figures are in every instance too low, but the product moment correlation for all 30 observations is as good as that for phosphorus and protein, and better than that for fat, which is based on only 21 observations for 3 subjects.

DISCUSSION

. These results would seem to warrant the conclusion that the qualitative method, as it is described above, is adequate for scoring a group of individuals and for comparing any one of the individuals with the group as regards ingestion of the various food elements. Obviously, the method is not applicable as a part of balance study technique. The method should be useful for studying the influence of nutritional factors on a large group of individuals. There is compensation for lack of precision in the fact that nutritional disorders are usually not noticeable until an individual deviates considerably from an optimum intake.

The reason for the low calcium scores is not entirely clear. No doubt there is a tendency for the qualitative method to underrate, but this is probably not the only reason, since one would anticipate an under-rating of all factors to take place simultaneously and not consistently only one of them. A significant part of this discrepancy is probably due to the very high calcium content of the water in this locality.

SUMMARY

The dietary habits of 25 individuals are described and compared. The variation in intake of a given food item or group of food items from one week to another is largely dependent upon the average quantity (number of servings) eaten in a week. It is pointed out that this fact may have some bearing on the question of changes in dietary

the serving of that group; multiply this product, which is the estimated quantity per week of that food group which was eaten, by the score for that food group (from the tables) for calcium, phosphorus, nitrogen, fat, etc., and divide by 100 (since the score is based on 100-gm. samples). The values for each food element thus determined are then added and the total estimated value for each food element is obtained. Those obtained for calcium, phosphorus, protein, and fat can be seen on Fig. 2. There the scores for two individuals are marked. These are

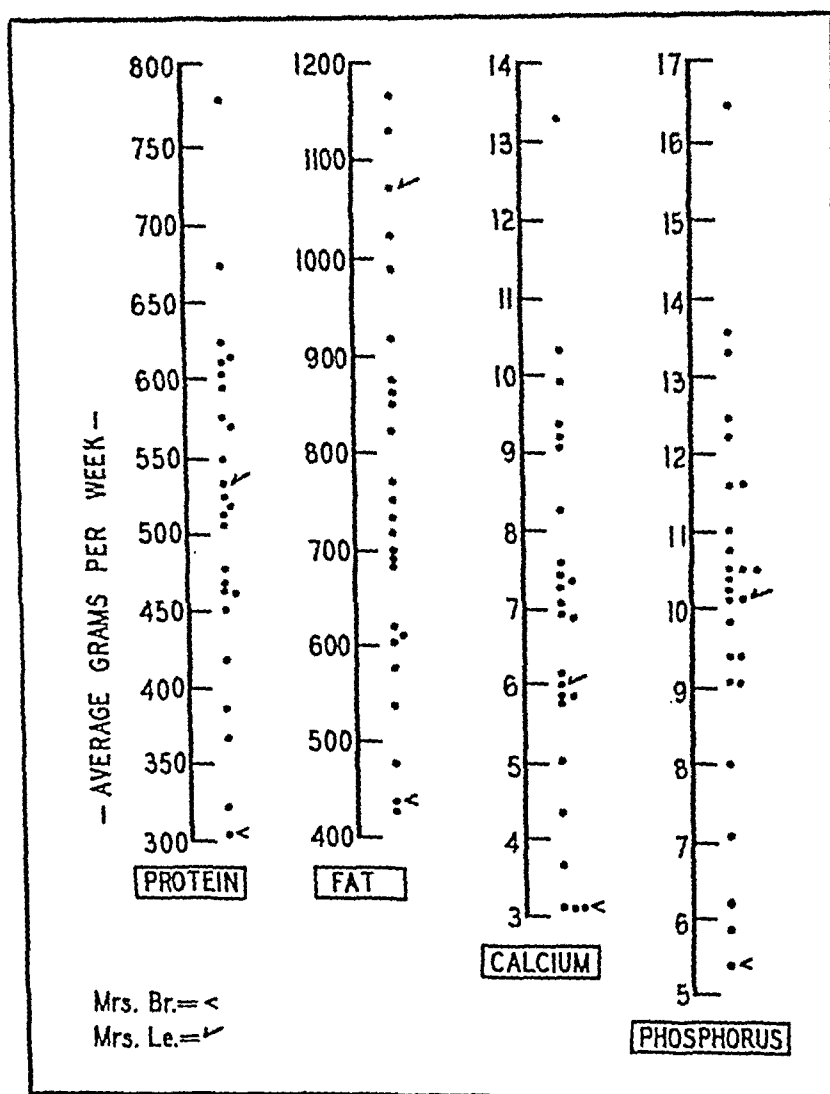


Fig. 2.—The estimated quantity of protein, fat, calcium, and phosphorus ingested per week by 25 women during pregnancy. The scores for Mrs. Br. and Mrs. Le. are indicated.

the same persons whose average number of servings per week have been followed through on Fig. 1. If the records of these two are examined on both figures it is not difficult to see why the habits of one of them (Mrs. Br.), as indicated on Fig. 1, should have resulted in such low intakes of protein, calcium, phosphorus, and fat as our estimates indicate in Fig. 2, since her general level of ingestion is low. The reason for the low calcium score and almost average intake of

to protect the perineum from serious laceration and also to protect the fetus from sudden increase in intracranial pressure. When episiotomy is indicated it should be performed soon after the presenting part has descended to the pelvic floor rather than when perineal laceration is imminent. This not only preserves the integrity of the pelvic floor but subjects the fetus to a lesser degree of trauma.

Technic.—Mediolateral episiotomy is the type in routine use at the Chicago Lying-In Hospital. The depth of the incision varies, of course, in the individual case but has usually been sufficiently deep to cut the superficial portions of the levator ani muscle. In nearly all instances the repair has been performed at the completion of the third stage of labor.

Two general methods of repair have been employed. In nearly three-fourths of the cases (72.6 per cent) nonabsorbable suture has been used. In this type of repair the edges of the vaginal mucosa are approximated with interrupted catgut suture. The muscle of the perineal body and the skin edges are brought together with deep interrupted, figure-of-eight, silkworm sutures. Usually four to six such sutures are used. They are tied loosely and at the completion of the repair the skin edges are accurately approximated and fixed with Allis clamps which are left in place for ten to fifteen minutes. This is the type of repair which the internes are instructed to use and which is routinely performed for teaching purposes.

TABLE I. CHICAGO LYING-IN HOSPITAL, JULY 1, 1933, TO JUNE 30, 1935

Total No. deliveries	5,624		
With episiotomy	2,987	52.9%	
Without episiotomy	2,637	47.1%	

<i>Episiotomy</i>			
	TOTAL	INFECTED	PER CENT
Silkworm-gut repairs	2,170	56	2.5
Catgut repairs	817	11	1.3

In the other method catgut is the primary suture material used. Either continuous or interrupted sutures are used to approximate the muscle and subcutaneous tissue. The vaginal mucosa is closed with catgut and the skin edge with either catgut or a subcuticular silkworm suture.

During the delivery particular attention is paid to hemorrhage from the episiotomy wound. This is usually controlled satisfactorily by the pressure of a sponge in the incision. Bleeding vessels are clamped and tied prior to delivery. During the repair any bleeding points are carefully ligated. The amount of blood loss may be considerable and hemorrhage is one of the dangers of episiotomy, difficult perhaps to evaluate but of undoubted importance.

Care of the perineum during the puerperium has been the same in the two types of repair. It consisted of perineal irrigations following voiding or defecation. Heat has been applied in the form of saline packs when discomfort is present. Careful inspection of the perineum is routine when any abnormality is suggested. The silkworm sutures are removed on the eighth postpartum day except when earlier removal may be indicated for drainage.

Immediate Results.—Healing of the episiotomy incision takes place with equal rapidity in the two groups. In the absence of infection there is no apparent difference in the amount of discomfort. Pulling of the sutures may occur in either group and the amount of soreness present depends to a considerable degree upon the tension used in tying the sutures. Ample room should be allowed for the edema which usually develops. Care should be exercised in tying the silkworm sutures so that the cut ends will not prick the skin surface.

habits during pregnancy. A system whereby the quantity of calcium, phosphorus, protein, etc., eaten is estimated from daily qualitative records of the food items eaten by an individual has been described and evidence is given to show that the system is reliable within such limits as are frequently desirable for certain types of group dietary studies.

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A STUDY OF 2,987 CONSECUTIVE EPISIOTOMIES

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AN OPERATIVE procedure which is frequently performed may gradually become ignored as a possible source of complications. This is particularly true if the procedure is undertaken only as a portion of the treatment of the patient. In many respects this is the present attitude toward episiotomy. This study was undertaken in an attempt to evaluate episiotomy from this standpoint. A comparison is also presented between two common methods of repair of episiotomy.

The material upon which this study is based was obtained from a review of the records of all patients delivered in the Chicago Lying-In Hospital from July 1, 1933 to June 30, 1935. During this period there were, 5,624 hospital deliveries. Episiotomy was performed in 2,987 of these deliveries (Table I). The incidence of episiotomy is therefore 52.9 per cent in this series. Slightly less than one-half of the total group of patients were being delivered for the first time. In nearly every instance the episiotomy was performed upon a primipara or upon a patient who had had a previous episiotomy.

Indications.—Episiotomy is usually performed in an attempt to minimize the injury to the birth canal which occurs with the passage of the presenting part and after-coming head over the perineal body. If the outlet is not enlarged by such a procedure, laceration occurs in 50 to 60 per cent of primiparas. Episiotomy becomes increasingly indicated when the perineum has less than the normal elasticity due to such conditions as advancing age, extreme muscularity, perineal scars, or congenital deficiencies. In the presence of a large or firm fetal head the danger of perineal rupture is increased. Contracted pelvis, particularly of the funnel type, necessitates a greater encroachment of the fetus upon the posterior part of the pelvic outlet and increases the frequency of perineal tears. Rapid delivery occurring before adequate dilatation of the soft parts has been accomplished indicates episiotomy

TABLE IV. TOTAL MORBIDITY

TYPE OF DELIVERY	NO. OF CASES	UPPER GENITAL TRACT INFECTION	INFECTED PERINEUM	FEMORAL THROMBOPHLEBITIS	UPPER RESPIRATORY INFECTION	URINARY TRACT INFECTION	MASTITIS	UNDETERMINED	MISCELLANEOUS	TOTAL MORBIDITY	PER CENT
Spontaneous	1,631	48	10	1	6	4	4	94	1 (Appendix)	168	10.3
Low forceps	1,029	34	17		14	3	3	65	1 (Anemia)	138	12.4
Midplane forceps	184	8	6	2	1	2	1	16	1 (Tuberculosis)	37	20.1
Midplane forceps with Dührssen's incisions	32	7	3		1			3	1 (Eclampsia)	14	43.7
Breech extraction or forceps on aftercoming head	75	3			1			9		13	17.3
Twins with interference	9	1						2		3	33.3
High forceps	10	3						3		6	60.0
High forceps with Dührssen's incisions	11	4	1					4		9	81.8
Version and extraction	5	1						1	1 (Tuberculosis)	2	40.0
Craniotomy	1									1	100.0
Total	2,987	109	37	3	23	9	8	197	5	391	13.1

Infection of the episiotomy wound was present in 67 patients of the total group. The incidence of infection is therefore 2.2 per cent. The incidence is slightly higher in those repaired with silkworm suture. In the 2,170 patients repaired in this manner 2.5 per cent (56) showed infection. In the catgut repair series 11 of the 817 patients (1.3 per cent) had infection in the wound (Table I). Many of the infections were of minor character as is evidenced by their relation to febrile morbidity. Interesting in this connection is the fact that in the silkworm group only one-half of the infected patients had sufficient elevation of temperature to be considered as morbid (Table II). In the catgut group, however, 9 of the 11 patients with infec-

TABLE II. MORBIDITY

	TOTAL	TOTAL NUMBER MORBID	PER CENT	MORBIDITY DUE TO EPISIOTOMY
Silkworm gut	2,170	278	12.8	28
Catgut	817	113	13.8	9

Follow-Up

	TOTAL	GOOD		FAIR		POOR		NO RECORDED	
		NO.	%	NO.	%	NO.	%	NO.	%
Silkworm gut	2,170	1,006	46.3	375	17.2	49	2.2	740	34.1
Catgut	817	336	44.8	49	5.9	9	1.1	393	48.1

tion were classed as morbid. It would appear that infection in the latter group was more extensive or that it was not as readily recognized so that early drainage could be established.

The incidence of infection shows, as would be expected, a correlation with the type of procedure used to complete delivery (Table III). Approximately one-half

TABLE III. OPERATIVE PROCEDURES

	TOTAL	SILKWORM-GUT			CATGUT		
		TOTAL	IN-FECTED	PER CENT	TOTAL	IN-FECTED	PER CENT
Spontaneous delivery	1,631	1,233	25	2.02	398	1	0.25
Low forceps delivery	1,029	687	14	2.03	342	8	2.31
Midplane forceps	184	136	10	7.3	48	-	-
Midplane forceps with Dührssen's incisions	32	27	-	-	5	-	-
Breech extraction or forceps on after-coming head	75	63	5	7.9	12	-	-
Twins with interference	9	8	-	-	1	-	-
High forceps	10	5	1	20.0	5	2	40.0
High forceps with Dührssen's incisions	11	9	-	-	2	-	-
Version and extraction	5	2	1	50.0	3	-	-
Craniotomy	1	-	-	-	1	-	-
Total	2,987	2,170	56		817	11	

of the episiotomies preceded natural delivery. The incidence of infection is lowest in this group and increases with the complexity of the obstetric procedure performed. It is to be noted that comparable numbers of the various operative procedures were done in the groups with the two types of repair. The incidence of low forceps deliveries was 31.6 per cent in the silkworm group and 40.8 per cent in the catgut group, while in midplane forceps, the figure was 6.2 per cent and 5.8 per cent, respectively. The other operative procedures show a similar parallel so that this is not a significant factor in the evaluation of the two methods of repair.

dent morbidity, incidence of infection, and end-results. We believe that a sufficiently large series has been summarized to eliminate the majority of errors which might be due to individual factors. The following conclusions are presented:

1. Infection of the episiotomy wound is a minor but significant cause of puerperal morbidity.
2. The incidence of infection is greater in those cases repaired with silkworm gut suture but the average infection in this group is less severe.
3. The incidence of infection in both types of repair increases rapidly with the complexity of associated obstetric procedures.
4. Morbidity and end results depend upon factors other than the type of suture material used in the repair.

FACTORS AFFECTING BLOOD LOSS IN THE THIRD STAGE OF LABOR*

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THE problem of blood loss in the third stage of labor has been subject to extensive statistical treatment in four different investigations, first by Ahfeld¹ in 1904, next by Calkins, Litzenberg, and Plass in 1929² and 1931³ and more recently by Pastore⁴ and the present writers.

These researches have much in common, inasmuch as they all utilize large numbers of cases. Pastore's series is the only one numbering less than 1,000 cases. They all consider the effects of such factors as gravidity, age of the mother, duration of labor, weight of the fetus, and weight and area of the placenta, and they note further the influence of the management of the third stage on blood loss.

Ahfeld and Pastore conclude that certain of the factors named have a marked influence on blood loss, whereas our work and that of Calkins indicate that, while such factors as weight of the mother, weight of the child, and weight and area of the placenta are significantly related to blood loss, the extent of the relationship is too small to be of any predictive value in individual cases.

The secret of the discrepancy lies in the statistical method used. Ahfeld and Pastore relied on a comparison of averages while the other

*Presented at a Meeting of the Minnesota Society of Obstetrics and Gynecology.

Morbidity.—The factors responsible for morbidity in the total group of 2,987 are recorded in Table IV. The standard of morbidity used is that suggested by DeLee. Every patient with a temperature of 100° F. at any time throughout the hospital stay is considered morbid. The morbidity rate for the 2,987 patients is 13.1 per cent using this standard. If classified according to the Strassburg method (any patient having a temperature of 100.4° F. on two days of the second to tenth puerperal days inclusive), the morbidity rate is lowered to 6.7 per cent. In Table IV the causes of morbidity and their frequency in the various obstetric procedures employed in the group are summarized. It is to be noted that infection of the episiotomy wound, although relatively infrequent, forms the second largest group of specific causes of morbidity. It is exceeded in frequency only by upper genital tract infection.

Morbidity may be considered by other standards than temperature elevation. An increase in the average duration of hospitalization should be classed as evidence of morbidity. The usual duration of hospital stay for our patients is ten days. In the group of patients in whom an infected episiotomy was present the period of hospitalization was somewhat longer. The average duration in the cases repaired with the silkworm gut technique, in which infection of the wound developed, was 12.5 days. In the patients in whom infection was present in an episiotomy wound repaired with the catgut suture technique the average duration of hospitalization was prolonged to 15.3 days.

Mortality.—In the complete series of 5,624 delivered during the period of our study there were 12 deaths. This results in a mortality rate of 21.3 per 10,000 patients. Only three of these deaths occurred in the 2,987 patients upon whom episiotomy was performed. In these three instances there is no demonstrable relation between the episiotomy and the fatal termination. In one of the patients pregnancy was complicated by severe mitral cardiac disease. She was delivered at term by episiotomy and low forceps operation. Death occurred one and one-half hours postpartum of cardiac decompensation. In the second case delivery at term was accomplished also by episiotomy and low forceps application. Death occurred six days postpartum of agranulocytic angina. The episiotomy was repaired with catgut suture and it showed no evidence of infection. The third patient was delivered following episiotomy and midplane forceps application. She died sixty-one days postpartum of puerperal sepsis. The episiotomy was repaired with silkworm suture and was infected. The perineal infection appeared to be secondary to an intrauterine infection with a profuse lochial discharge from which hemolytic streptococci were cultured.

End-Results.—An attempt was made to determine the character of perineal support following episiotomy as evidenced by the condition at the time of examination at least six weeks postpartum. Information was available in the records of 62.1 per cent of the total group with a slightly higher incidence of follow-up in the silkworm gut repair group than in those repaired with catgut. Table II shows a classification of results in the two types of repair. It is to be noted that a poor result was recorded in 2.2 per cent of the silkworm repair group and in 1.1 per cent of the catgut suture repairs. No significant difference in the end-results of the two groups could be noted and generally satisfactory results were recorded. Occasional instances were recorded in both groups in which over-approximation of the incision had been produced. This error is a source of dyspareunia which may not be relieved until the vaginal opening is enlarged by superficial incision. It is to be differentiated from pain due to tenderness along the line of the episiotomy tear. Such tenderness may persist for several months and then gradually disappear.

SUMMARY

Two thousand nine hundred and eighty-seven consecutive episiotomies have been considered from the standpoint of immediate healing, coinci-

Using a modification of Williams' technique, Calkins in 1929 was able to reduce the average blood loss to 222 c.c. Calkins, Litzenberg, and Plass, were also interested in factors other than management affecting blood loss in the third stage, and they are the authors of an interesting paper on the subject. Calkin's contribution is based on 1,400 University hospital cases, Plass's on 1,200 private patients, and Litzenberg's on 3,000 University hospital cases.

Using both the comparison of averages and the correlation method, they found that the age of the mother bore no relation to blood loss, but that, due to lacerations, a first pregnancy resulted in slightly greater blood loss than subsequent pregnancies. The length of the third stage of labor was more closely related to blood loss ($r = 0.14$) than the first or second stage ($r =$ about 0.05). Such factors as height and weight of the child and the mother and weight and area of the placenta seemed to have more effect on blood loss since their correlation ranged from 0.09 to 0.18. The management of the third stage was probably more important than any of the other factors, one investigator reporting an average loss of 462 c.c., whereas the other two found average losses of 317 and 222 c.c.

Pastore's study reports an average blood loss of 244 c.c. which compares favorably with the Calkins figure, but Pastore is also to be criticized for not using the correlation technique. His method, the comparison of averages, is the same as that of Ahfeld, done thirty-two years before and his series of cases is not nearly as large. He does, however, include such additional factors as the effect of time of rupture of the membranes, type of presentation of the placenta, and degree of laceration on blood loss. He agrees with Calkins in concluding that duration of labor, weight of the baby, and weight of the patient are related to blood loss, but due to his use of averages he overestimates the amount of the relationship. For the same reason, he stresses the relation between blood loss and age which is really insignificant, and although he gives no figures, he states that there is no relation between weight and area of the placenta and blood loss.

The present study is based on an analysis of 1,658 births at the Minneapolis General Hospital not including multiple births, cesarean sections, and certain incomplete records. Premature and operative deliveries are included with the other cases. The statistical constants have been calculated separately for premature infants, i.e., those weighing under 2,800 gm.; normal infants, i.e., those weighing over 2,800 gm.; and for the total group which had an average weight of 3,348 gm. Since the correlations with blood loss are substantially the same for all three divisions, only the figures for the total group will

studies used the correlation^c technique. Comparison of averages may magnify the relationship, since it does not take into account the amount of overlapping between groups. If the number of cases is large, a very small correlation will account for consistent difference in averages. The correlation method takes account of the variability and gives the amount of the relationship in a single figure.

For example, consider Table I taken from Pastore, showing the relationship between age and blood loss in the placental stage.

TABLE I. AGE OF MOTHER AND BLOOD LOSS (FROM PASTORE)

AGE	NUMBER OF CASES	AVERAGE BLOOD LOSS
Less than 20	33	183 c.c.
20-29	337	220 c.c.
30-34	79	266 c.c.
Over 34	51	279 c.c.

Since the average blood loss increases consistently with age, Pastore concludes that there is a significant relationship, that is, that older women lose more blood than younger women. As a matter of fact, if a scattergram were made with age as one axis and blood loss as the other, and points plotted indicating the age and the blood loss for each woman, they would be so scattered that they would show no definite trend. Calkins and the present writers all find correlations of 0.01 or 0.02 for these variables, and if Pastore's data are assumed to have the same variability as ours, a correlation biserial r_t of 0.15 is obtained, which might result by chance from a truly zero relationship.

Since Ahfeld's work was done before the correlation technique was known, he is justified in not using it. Ahfeld noted the effect of gravidity, weight of the child, weight and surface area of the placenta, and length of labor on blood loss. He found a greater blood loss to be associated with a heavier child, a larger placenta, or a longer labor. In his management of the third stage, unless the patient had a hemorrhage, he usually did not attempt placental expression until two hours had elapsed.

Williams,⁵ in 1919, criticized Ahfeld's technique of management which resulted in an average blood loss of 515 c.c. He reported that his method of expressing the placenta from the vagina by gentle pressure upon the fundus immediately following placental separation, resulted in an average blood loss of only 344 c.c.

^cThe coefficient of correlation, Pearson's r , is measured by the formula $r = \frac{\sum xy}{\delta_x \delta_y}$ where x is a deviation from the mean value of all the x 's, y is likewise a deviation from its mean, and δ_x and δ_y measures of variability or spread are $\sqrt{\frac{\sum x^2}{N}}$ and $\sqrt{\frac{\sum y^2}{N}}$, respectively. r is -1 if x and y have a perfect inverse relationship, +1 if x and y have a perfect positive relationship, and 0 if the association between x and y is what would be expected by chance.

[†]Biserial r is used as a measure of correlation if one variable, such as blood loss, is in quantitative form, but the other is divided into two categories, such as age under thirty and age over thirty. Biserial $r = \frac{M_1 - M_2}{\sigma} \frac{pq}{z}$ where M_1 and M_2 are the means for the two categories, p and q are the percentage in each, and z is the ordinate of the normal curve at the point p . σ is the standard deviation as previously defined.

Total length of labor exerts a small but significant* influence on blood loss as indicated by an r of 0.07. However, when the three stages of labor were considered separately by Calkins and his co-workers, they found the third stage to be a little more closely related to blood loss than was the first or second.

Height and weight of the mother are related to blood loss to a similar extent, height correlating 0.07 and weight 0.05. Calkins found slightly higher correlations for these factors, i.e., 0.12 for height and 0.16 for weight. On the average, then, the tall heavy woman may be expected to lose more blood than the short thin one, but in any individual case no estimate of blood loss can be made from the height and weight of the patient.

The blood pressure of the patient is not at all related to blood loss, since the correlation is -0.02 for systolic and exactly zero for diastolic pressure.

Weight of the child correlates 0.14 with blood loss. Litzenberg found this correlation to be 0.21 for first pregnancies and 0.11 for succeeding pregnancies. There is an average tendency for a heavier first born baby to be associated with a greater blood loss.

Similar results are found by correlating the placental dimensions with blood loss, as indicated by a correlation of 0.16 between weight of the placenta and blood loss. Here, too, Litzenberg found the association to be closer ($r = 0.18$) in primiparous women than in multiparous ($r = 0.10$), so that especially in first pregnancies a heavier placenta is associated with a greater blood loss. A larger placenta also goes with greater blood loss as indicated by a correlation of 0.14 between area of the maternal surface of the placenta and blood loss. Area was determined by tracing the periphery of the placenta on heavy paper and then measuring the area by a planimeter. Our correlation of 0.14 is a little higher than 0.10 reported by Litzenberg. Ahfeld's early contention that weight and area of the placenta are associated with blood loss is borne out by the present study, but one must remember that a large placenta and greater blood loss need not necessarily go together in individual cases.

An analysis of the effect of the type of presentation of the infant and type of presentation of the placenta on blood loss is presented in terms of averages, but if the large variability (of 209 c.e.) is kept in mind these average differences must be interpreted with caution.

The Schultz type of presentation of the placenta, occurring in 70 per cent of the cases is associated with an average blood loss of 203 c.e. while the Duncan type, occurring in 30 per cent of the cases, gave

*When the number of cases is over 1,000, r of 0.06 or over is probably significant: that is, in other samples of similar size a positive correlation will result again.

be considered in detail. Reference to Table II will show the averages, standard deviations and correlations with blood loss for normal infants. Table III gives the corresponding information for the total group.

The average blood loss, as measured by our technique, was 223 c.c. with a standard deviation of 209 c.c., so that about two-thirds of the patients lost between 14 and 432 c.c. of blood.

TABLE II. MEANS AND STANDARD DEVIATIONS FOR VARIOUS FACTORS AND CORRELATIONS WITH BLOOD LOSS FOR NORMAL INFANTS

FACTOR	NUMBER OF CASES	MEAN	STANDARD DEVIATION	R WITH BLOOD LOSS
Blood loss	1,427	220 c.c.	211.3 c.c.	----
Age of mother	1,362	27 yr.	6.5 yr.	0.02
Gravidity	1,427	3	2.5	-0.03
Length of labor	1,329	12 hr.	11.3 hr.	0.09
Height of mother	1,026	63 inch.	2.3 inch.	0.06
Weight of mother	1,026	135 pounds	22.7 pounds	0.05
Systolic blood pressure of mother	1,362	124	14.5	-0.01
Diastolic blood pressure of mother	1,362	81	11.4	0.00
Weight of child	1,427	3533 gm.	429.8 gm.	0.14
Weight of placenta	1,427	619 gm.	135.9 gm.	0.13
Area of placenta	1,427	44 sq. in.	8.3 sq. in.	0.13

TABLE III. MEANS AND STANDARD DEVIATIONS FOR VARIOUS FACTORS AND CORRELATIONS WITH BLOOD LOSS FOR TOTAL GROUP

FACTOR	NUMBER OF CASES	MEAN	STANDARD DEVIATION	R WITH BLOOD LOSS
Blood loss	1,658	223 c.c.	208.5 c.c.	----
Age of mother	1,580	27 yr.	6.5 yr.	0.01
Gravidity	1,658	3	2.6	-0.03
Length of labor	1,544	12 hr.	11.2 hr.	0.07
Height of mother	1,176	63 inch.	2.3 inch.	0.07
Weight of mother	1,176	134 pounds	22.5 pounds	0.05
Systolic blood pressure of mother	1,580	124	15.7	-0.02
Diastolic blood pressure of mother	1,580	81	12.0	0.00
Weight of child	1,658	3348 gm.	642.7 gm.	0.14
Weight of placenta	1,658	599 gm.	141.3 gm.	0.16
Area of placenta	1,658	43 sq. in.	8.9 sq. in.	0.14

Like Calkins, we found that age is not related to blood loss since the correlation between these factors is only 0.01. Litzenberg found that the correlation is still approximately zero when only first pregnancies are considered, so that the lack of correlation is not due to the obscuring effect of gravidity. Gravidity itself has a slight negative correlation, -0.03, with blood loss. Parity, according to Calkins, correlates -0.05. Thus, there is indicated a barely noticeable tendency for succeeding pregnancies to be associated with smaller blood loss.

THE EFFECT OF CERTAIN SEDATIVES AND ANALGESICS ON UTERINE CONTRACTIONS

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THE common belief that opiates induce a certain degree of uterine relaxation which tends to prolong normal labor, as well as to expose the parturient to an increasing hazard of postpartum hemorrhage, led us to undertake a study of the effect of various sedative and analgesic drugs on uterine motility.

Our object was to establish a record of normal uterine contractions during the first and second stages of labor and to observe the alterations, if any, in these contractions in response to the administration of sedatives.

Various methods for recording uterine activity by means of external appliances fixed to the abdominal wall have appeared in the literature¹⁻⁵ from time to time and have rapidly fallen into disfavor with researchers who tested them.

In 1932 Dodek described a new method of external hysterography.⁵ In our hands so far it has proved unsatisfactory. We have reproduced the apparatus in every detail but have failed to obtain a record of uterine contractions during labor simulating that published by Dodek. The principle upon which the apparatus is based is that "during each uterine contraction the anteroposterior diameters of the uterus and the maternal abdomen are increased. The more severe the contraction the greater is the increase." We have observed that in the first stage of labor the patient frequently complains bitterly of pain but no evidence of change in abdominal contour occurs, and the apparatus fails to register the uterine contraction that has apparently taken place. Extraneous movements, however, such as deep breathing, coughing, movements of the trunk and lower limbs, are recorded. Very strong uterine contractions influence the device, but the record obtained does not permit a true interpretation of the extent and force of the uterine contractions.

The German worker, Rech,⁶ in 1934 reported the use of an electromechanical hysterotonograph. Some such a method may possibly provide in the future a means of investigation. The last word on external hysterography has not, as yet, been said.

It remained, therefore, for us to continue along the same lines of investigation as previously reported from this clinic for the study of oxytocic drugs.

Though no positive conclusions can be assumed from the contrast of the action of the drug on the postpartum uterus with that on the uterus during labor, it is interesting to note the behavior of this muscular organ in the puerperium. Without having tracings obtained during labor it is mere speculation to assume that a similar response might be obtained from the intrapartum case.

an average blood loss of 270 c.c. Pastore, also, found the Duncan type to be associated with a somewhat greater blood loss.

The type of presentation of the infant, however, has practically no relation to blood loss (as shown by Table IV).

TABLE IV. BLOOD LOSS IN THE THIRD STAGE AND TYPE OF PRESENTATION OF THE INFANT

TYPE OF PRESENTATION OF THE INFANT	NUMBER OF CASES	AVERAGE BLOOD LOSS C.C.
O.L.A.	858	230
O.R.A.	617	219
O.L.P. and O.R.P.	93	212
Breech	48	196
Chin and shoulder	14	179

SUMMARY

Of all the factors studied, none has any marked relation to blood loss. The age of the mother, her blood pressure, and probably her gravidity have no measurable effect; the height and weight of the mother and the total length of labor have a very small but significant relation. The weight of the infant and the weight and area of the placenta are related a little more closely to the blood loss. On the average, the tall heavy woman who has a long labor will lose more blood than the short thin woman who has a short labor. On the average, too, a large baby and a large placenta will result in a greater loss of blood than will a small baby and a small placenta.

Not one of these factors, however, approaches the importance of the management of the third stage of labor in its effect. For it is through improved technique of management that the average blood loss has been reduced from over 500 c.c. at the beginning of the century to about 225 c.c. at the present time.

We wish to acknowledge our indebtedness to Dr. John A. Urner of the Minneapolis General Hospital under whose direction the clinical data for this study were collected.

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creases the danger of subsequent respiratory depression of the baby because of our inability to plan the optimum time of administration to accord with the time of delivery.

EFFECT OF SEDATIVES ON UTERINE MOTILITY

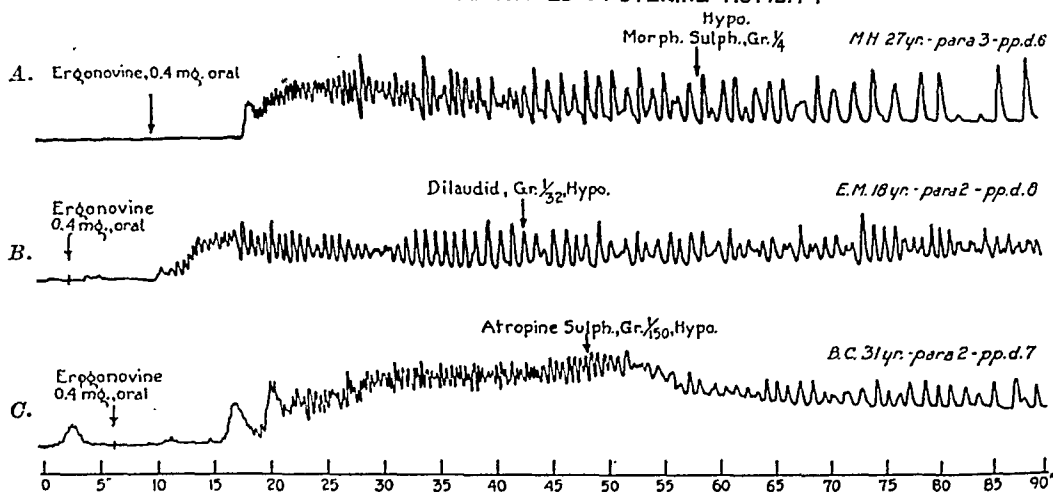


Fig. 1.

Atropine sulphate, $\frac{1}{150}$ gr. given hypodermically, caused a slight fall in the general tone of the uterus (Fig. 1-C). Other workers have observed similar results. The contractions became slightly lower in amplitude, but the uterine activity was never completely abolished. Atropine when used in combination with morphine apparently does not have the power to relax the uterus to any appreciable degree.

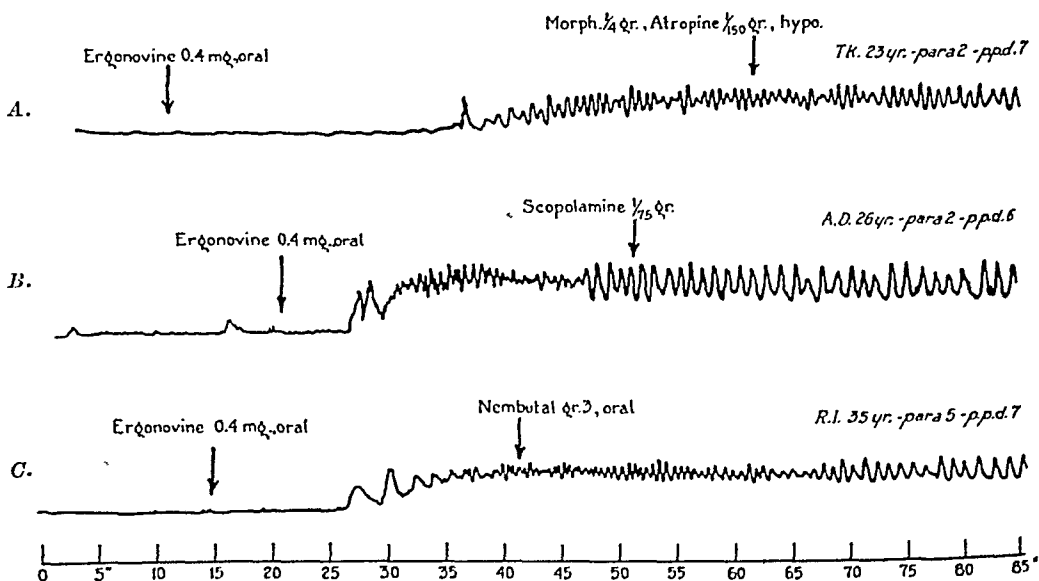


Fig. 2.

Scopolamine given alone in doses of $\frac{1}{200}$, $\frac{1}{100}$, or $\frac{1}{75}$ gr. has a tendency to relax the uterus more or less between individual contractions (Fig. 2-B). A similar effect is noted when it is given in combination with morphine. This may be a causative factor in the prolongation of the first stage of labor if the drug is administered too early. But here again, an analogy between the uterus during labor and that of our

For our observations postpartum patients from the sixth to the eighth day were used. Multiparas who had no perineal tears and had had an afebrile course lent themselves most favorably to the study of uterine motility.

The small rubber bag was introduced into the uterine cavity with strict aseptic precautions. After an initial period of observation, during which the uterus was found to be inactive, uterine motility was initiated by the administration of an oxytocic substance. Ergonovine, orally or intravenously, in 0.4 and 0.2 mg. doses respectively was used. In all cases the activity of the uterus was registered promptly. It was marked by a rapid rise in the tone of the organ, followed by a brief period of tetany which, in turn, was succeeded by intermittent, regular, uterine contractions. These contractions often became successively greater in amplitude as the activity continued. The general tone of the uterus remained above the initial level.

Having established a record of the uterine motility, we proceeded to observe the influence of sedatives given subcutaneously and of analgesics administered orally.

Morphine sulphate, $\frac{1}{4}$ gr. hypodermically produced no appreciable change in uterine motility (Fig. 1-A). The tone was unaffected. It remained constant. The amplitude of the contractions was unchanged in the greater number of cases, while in a lesser number there occurred an increase in the height of the contraction. This phenomenon is frequently seen in the patient who has uterine contractions initiated by ergotrate. The interval between the individual contractions after the administration of morphine was slightly prolonged, indicating a degree of relaxation although the general tone was unchanged. Subjectively the patient experienced nausea and faintness.

Morphine $\frac{1}{4}$ gr. combined with atropine $\frac{1}{150}$ gr. gave similar results. In only two out of ten instances was the regularity of the uterine contractions somewhat altered (Fig. 2-A).

From the tracings obtained one may conclude that the tone and activity of the postpartum uterus are not significantly affected by morphine. How far this holds true for the uterus in labor one cannot state positively. Our observations suggest that the possibilities of extreme relaxation and increased postpartum hemorrhage due to its use as intrapartum and postpartum medication are slight in the absence of deep inhalation anesthesia. The fact that uterine contractions continue regularly and uniformly after the administration of morphine lends further support to the idea that its use during labor secures some analgesia while the uterus continues its normal function, provided there is analogy between the reaction of the postpartum and intrapartum uterus.

However, the ill effect of the drug on the respiratory mechanism of the baby must be borne in mind. Therefore, the optimum dose and the time of its administration during labor should be carefully considered. The uncertainty of the time of delivery, especially in a multipara, in-

ORAL PARALDEHYDE IN OBSTETRICS

FURTHER REPORT OF 300 ADDITIONAL CASES

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IN A RECENTLY published article, two of the authors reported a preliminary study of 50 cases in which paraldehyde was given per os as an obstetric analgesic, and at this time we wish to present the results of 300 additional patients receiving oral paraldehyde during labor. We also desire to present a more simplified technic than that originally used.

In this series the paraldehyde was combined with aromatic elixir instead of the propylene glycol, alcohol, and syrup of acacia mixture, the result being that the total quantity to be swallowed was much smaller, nausea and vomiting were much less frequent and the taste was as effectively disguised. *Elixir aromaticum U.S.P.* (simple elixir) is a syrup almost universally used as an agent to improve the taste of liquid medicines; it is easy to procure, inexpensive and perfectly harmless, and in our hands has proved a most satisfactory vehicle for paraldehyde.

TECHNIC

It is no longer considered necessary to wait for any particular amount of cervical dilatation or descent of the presenting part before beginning analgesia, the desire of the patient for relief from pain being the main indication. She is told that she will be given something as soon as she wishes it and is cautioned not to wait too long before seeking relief, otherwise it may be given too late for her to receive the full benefits. Better results are obtained when the paraldehyde is preceded by either $1\frac{1}{2}$ to 6 gr. of pentobarbital sodium, the usual dose being 3 gr., or $\frac{1}{6}$ to $\frac{1}{3}$ gr. of pantopon, it being remembered that the two drugs should not be given in combination. Usually about one hour is allowed to elapse after the preliminary medication before giving the paraldehyde mixture, although this is not absolutely necessary and may be disregarded if labor is progressing quite rapidly. The paraldehyde and aromatic elixir are given in equal parts, the amount ranging from 4 to 6 drams each, the average being 5 drams, the dosage not varying with the age, size, or parity of the patient. The two are stirred briskly and the patient permitted to smell of the mixture or told that the odor and taste are pungent and slightly breath taking. The nostrils are loosely plugged with cotton and the patient is instructed to swallow the dose quickly; she is then given a few swallows of water and permitted to lie down and after a few minutes the cotton is removed from the nares.

If, as happens in a few cases, the patient is nauseated and regurgitates the mixture, an interval of about fifteen minutes is allowed and the administration repeated. In attempting to decrease nausea it is helpful to have the patient breathe

test patient may not hold. The conditions obtaining in each instance are different. Here we are judging quality rather than force of contractions. However, there was certainly no inhibition of activity.

Nembutal, used orally in 3 gr. doses, produced no appreciable change in the uterine activity (Fig. 2-C). The general tone and amplitude of the contractions were unaltered. There was, however, a slight lengthening of the interval between the individual contractions. The analgesic effect of the drug was well demonstrated. While the tracings showed as strong uterine activity as before the administration of the drug, the patient received definite relief from the pains.

Aspirin and codeine did not alter the uterine contractions. Dilaudid, $\frac{1}{32}$ gr. given hypodermically lessened the uterine contractions slightly (Fig. 1-B). The interval between the individual contractions was somewhat lengthened. No diminution in the general tone of the uterine muscle occurred. One is led to suspect that no relaxation of great degree occurs as a result of this drug in the above dosage.

SUMMARY

The method of internal hysterography furnishes the best method for study of uterine activity. Patients in the immediate postpartum period were observed. Uterine activity was initiated with ergonovine and the action of certain drugs commonly employed during labor was studied. While the force of the uterine contractions was not measured, the graphs show what changes were noted.

Further studies along these lines are needed and a safe and sound method for recording uterine activity during labor must be evolved in order that observations on the action of drugs during parturition may receive a direct interpretation and be valuable for clinical application.

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Pignoli, Renato: A New and Rapid Test for Syphilis, *Riv. ital. di ginec.* 19: 311, 1936.

The author describes the technique of a new test for the diagnosis of syphilis, using only a drop of dried blood, (Chediak-Dahr). The advantages of this method over the common diagnostic tests for syphilis are threefold: economy, simplicity, and rapidity. The report is based on 250 confirmed syphilitic patients and 125 confirmed nonsyphilitic patients. The author states that this test is especially valuable when an urgent blood transfusion becomes necessary.

AUGUST F. DARO.

TABLE II. METHOD OF DELIVERY

METHOD	PRIMIGRAVIDAE	MULTIGRAVIDAE	TOTAL
Spontaneous	2 (1%)	69 (62%)	71 (23.5%)
Low forceps	175 (91.5%)	35 (32%)	210 (70%)
Midforceps	10 (5%)	4 (4%)	14 (4.5%)
Breech extraction	5 (2.5%)	2 (2%)	7 (2%)

A number of additional operations were also done as the majority of patients had a routine cervical inspection following delivery with repair of any laceration; and a number of multigravidae with relaxed vaginal outlets had a posterior repair (elective perineorrhaphy) following delivery. All of the additional operations are enumerated in Table III.

TABLE III. ADDITIONAL OPERATIONS

Episiotomy	202
Perineorrhaphy elective	35
Trachelorrhaphy	54
Hysterostomatomy	4

Supplementary anesthesia was necessary for operative deliveries. Inhalation (N_2O-O_2 or ether) was used unless contraindicated, but always in greatly reduced amounts. The operative delivery of patients in whom inhalation anesthesia was contraindicated and the majority of elective perineorrhaphies were carried out under local infiltration and pudendal block. No supplementary anesthesia was required in the normal spontaneous delivery.

RESULTS AND DISCUSSION

The disagreeable taste and odor of oral paraldehyde were disguised by aromatic elixir. Five drams of paraldehyde and 5 drams of the elixir were given at the initial dose. No patients refused the mixture when it was offered to them and none complained of its unpleasantness. Their description of the drug was wide and varied and the greater majority definitely stated that they did not mind taking it at all. Amnesia began in ten or fifteen minutes and was complete in twenty or thirty minutes, complete amnesia being obtained in 94.3 per cent of the cases. Since we have begun to give the mixture earlier in labor the duration of amnesia before delivery has been increased. Primigravidae averaged three hours and thirty minutes without memory before delivery (minimum of one hour and maximum of eleven hours). Multigravidae averaged two hours and thirty minutes (a minimum of thirty minutes and a maximum of three hours) of amnesia before delivery. All patients slept for a few hours following delivery and drowsiness with unconcern and disorientation persisted for several hours.

deeply. The paraldehyde, elixir, and glass used should be kept in the ice box, for chilling aids materially in eliminating the slight burning sensation and reduces the odor by decreasing the volatility of the paraldehyde.

SERIES UNDER STUDY

The present study consisted of 300 cases, all of which were observed shortly after the onset of labor and none was especially selected. Approximately one-third of the cases were private and the other two-thirds divided equally between white and colored ward patients. The number of primigravidae as compared to multigravidae was almost 2 to 1, there being 191 and 109, respectively. Ages ranged from thirteen to forty-eight, the greatest number being between twenty and twenty-five years.

As in the previous study and for the same reasons considerable pathology was seen. The various complications and frequency of their occurrence are noted in Table I.

TABLE I. COMPLICATIONS

	NO. CASES
Preeclampsia	34
Chronic nephritis	14
Cardiovascular disease	3
Acute upper respiratory infection (on admission)	28
Antepartum pyelitis	5
Marginal placenta previa	2
Retained placenta	1
Hydramnios	4
Bicornute uterus	1
Congenital dislocation of hip	1
Bronchopneumonia	1
Twin pregnancy	2
Presentation face	1
Transverse arrest	6
Presentation breech	7
Presentation occiput posterior	25
Total	135

No particular attention was paid to the station of the presenting part at the time the paraldehyde was administered. The cervical dilatation averaged 5.5 cm. in the multigravidae and 6.2 cm. in the primigravidae at the time the drug was given. Elective low forceps and episiotomy were done routinely upon all primigravidae when the head reached the perineal floor and the cervix was completely dilated, a procedure also carried out in multigravidae who had had an episiotomy at former delivery. There were 25 occipitoposterior presentations at the time of delivery, 14 of which were delivered as such, 10 were manually rotated and 1 was delivered by the Seanzoni maneuver. Four cases of transverse arrest were delivered by low forceps and 2 by midforceps.

Pulse, respiration, and blood pressure are not changed in any great respect as compared to the normal case. There is a definite lowering of the blood pressure in all cases of hypertension, but not in the normal case, and we are convinced that there is great value in using paraldehyde in patients suffering from preeclampsia and eclampsia. We have seen paraldehyde lower blood pressure in cases where other drugs have failed, and it is our policy to use it whenever possible in hypertensive cases. No alarming drop of blood pressure was noted in any single case which could not be accounted for by her type of delivery or shocking procedure she received.

Blood loss not discussed previously has been carefully considered in this series, because of the fact that a number of questions are always raised as to whether or not paraldehyde has an ill effect upon uterine tone. The average blood loss for each case was 240 c.c. Five patients were considered as having had postpartum hemorrhage (500 c.c. or more). One was a case of multiple pregnancy with polyhydramnios and retained placenta. The blood loss was estimated as 1,200 c.c. Another patient had an extensive cervical laceration and lost an estimated amount of 1,000 c.c. The other three hemorrhages were of 500, 600, and 700 c.c. quantities and were attributed to partial uterine atony. All patients responded well to intravenous oxytocics, fluid, and blood and all made uneventful recoveries. We can thus say that paraldehyde has not increased the incidence of postpartum bleeding.

Nausea occasionally occurred after paraldehyde was given and vomiting only seldom. Thirty-eight patients vomited the initial dose and 34 of these retained a second dose given ten or fifteen minutes later. A number of patients who had prolonged labor required the administration of a second or third dose, the amounts being smaller than originally given. This was done without difficulty and no harm apparently resulted to baby or mother. There were in the series 22 patients who received this additional oral paraldehyde. There were 20 failures (6.6 per cent); 6 due to vomiting, 5 due to rapid labor, and 9 in which patients received only relative or partial amnesia.

There were no maternal deaths in this series. One patient aspirated vomitus at the time of nitrous oxide induction, developed a postoperative bronchopneumonia and ran a febrile course for a few days. Morbidity was present in 10.6 per cent of the patients, all of them being subacute and discharged from hospital in good condition.

All babies were carefully observed and of the 302 births, 8 were premature and 294 full term. Twenty-six of the full-term babies required moderate resuscitation before breathing was thought to be regularly and independently established. Five of the babies were sleepy in the nursery for twelve hours and several had the odor of paraldehyde on their breath for six to eighteen hours, but none of the babies exhibit-

The patient laboring under the influence of paraldehyde is sleeping, she rolls about with each contraction and utters an occasional groan. Sideboards on the bed are all that is necessary to keep her from harming herself, and someone in constant attendance, while advisable, is not needed, and the individual present need not be a physician or nurse, but merely someone to prevent the patient from rolling out of bed when the sideboards are not available. Restlessness of any undue degree is practically never seen, nor is restraint ever necessary.

The average duration of labor for the primigravidae was fifteen hours and six minutes (a maximum of thirty-six and a minimum of four). Multigravidae averaged nine hours and thirty minutes (a maximum of twenty-five and a minimum of two and one-half (see Table IV).

TABLE IV. DURATION OF LABOR

HOURS	PRIMIGRAVIDAE	MULTIGRAVIDAE	TOTAL
0-10	70 (36%)	56 (51%)	126 (42%)
10-20	79 (41%)	51 (47%)	130 (43.5%)
20 plus	42 (23%)	2 (2%)	44 (14.5%)

In the original paper it was stated that no oxytocics were used during labor, and that a temporary decrease in the intensity of uterine contractions was observed for a few minutes following the administration of paraldehyde. In this series 12 patients received 2 or 3 minims of pitocin intramuscularly to increase the uterine contractions. No frank case of uterine inertia was observed but these patients that received oxytocics were not having the expected type of labor. Pitocin thus administered did not have ill effects and the desired objective was obtained.

The number of spontaneous deliveries appearing is rather small, however 69 or 62 per cent of the 109 multigravidae delivered spontaneously. Taking into consideration that elective low forceps were used in all primigravidae and in multigravidae having had former episiotomy, the corrected percentage of multigravidae delivering spontaneously (72 per cent) is convincing that operative interference is not absolutely necessary. The expulsive efforts of the mother are present and not decreased, and the efficacy of the drug as an analgesia in the home established, although a word or two of caution is necessary if it is to be used in these surroundings; it must be remembered that the patient is asleep and the progress of labor cannot be determined by watching her and observing the intensity of her pains, and the labor is likely to be shorter than if she had not received relief. Therefore closer supervision by the physician is necessary and the progress must be determined by abdominal palpation and rectal examination.

A WORKING CLASSIFICATION OF ADNEXAL CYSTS AND NEOPLASMS*

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THE adnexa are real hotbeds of cysts and neoplasms, both benign and malignant. They are also frequent sites of inflammation, and the inflammatory mass often is difficult to differentiate clinically from benign or malignant cysts or neoplasms. The changes, which are numerous in the ovary, continue from puberty to after the menopause; this factor, together with the fact that the ovary contains many types of undeveloped cells and embryonic rests, may account for the high incidence of neoplasms. On account of the multiplicity of the lesions which affect the ovaries, parovarium and Fallopian tubes it is helpful in diagnosis and treatment to classify them by a simple, clear and concise method.

SIMPLE OVARIAN CYSTS AND INFLAMMATORY LESIONS

The age at which a patient submits herself for a pelvic examination is often important in determining the type of lesion under consideration. For example, it is more common to encounter inflammatory lesions in the third and fourth decades of life than in any other period. A mass which involves the adnexa at this time, and which is more or less cystic and tender to palpation, is likely to be an inflammatory, tuboovarian cyst. If some involvement is palpated on the other side, the diagnosis becomes more certain and treatment is readily advised. In delayed cases, when a tuboovarian cyst becomes definitely established, it may reach large proportions and become difficult to distinguish from an ovarian cyst. Even when the abdomen is open at operation the diagnosis may not be obvious, but when sacculated accumulations of serous fluid (inflammatory cysts) are situated over the uterus, broad ligaments and cul-de-sac the diagnosis of an inflammatory lesion can be made with reasonable certainty.

Simple cysts are also more common in the young than in the older individual, since the greatest physiologic activity of the ovary is at the lower ages. Fortunately, the majority of these cysts rupture spontaneously; this occurrence may be characterized by indefinite lower abdominal distress for twelve to twenty-four hours. Occasionally this

*Read before the meeting of the Minnesota Society of Obstetrics and Gynecology, Rochester, Minn., April 17, 1937.

ing these effects were a source of concern and all went through a normal neonatal period. We do not believe that paraldehyde is harmful to the full-term baby. Four of the 8 prematures required resuscitation by means of intratracheal aspiration and insufflation, the other 4 cried immediately and required no resuscitation. The concentration of the drug upon the vital centers in the premature seems to be more profound but not dangerously so. The gross fetal mortality was 5; 1 baby died eight hours after birth, and postmortem examination revealed massive congenital atelectasis and the odor of paraldehyde upon all viscera. While death may be attributed to paraldehyde, it is our impression that the occurrence of this condition might be seen in any normal series of this size. The second, a stillborn following a prolonged second stage caused by a face presentation, was autopsied and found to have intracranial hemorrhage. The third occurred in a patient with chronic nephritis, was a stillborn infant, and the fetal heart was not heard upon admission. The fourth was a case of a true knot* of the umbilical cord with evidence of gangrene at the proximal end and again fetal heart was not heard upon admission. One premature baby died on the sixth day the cause of death being prematurity and septicemia.

CONCLUSIONS

1. The use of oral paraldehyde as an obstetric analgesia is definitely established.
2. Oral paraldehyde can be satisfactorily administered in equal parts with aromatic elixir.
3. There are no contraindications to paraldehyde in labor.
4. Expulsive efforts of the mother are not diminished or abolished.
5. Complete amnesia is obtained in over 90 per cent of the cases.
6. Oral paraldehyde does not prolong the duration of labor.
7. There are no detrimental effects upon the mother.
8. There is a definite lowering of the blood pressure in hypertensive cases and the drug is recommended for the handling of preeclampsia and eclampsia.
9. There is no increase in postpartum bleeding.
10. No fetal deaths in this series can be attributed to paraldehyde.
11. It is perfectly safe for use in the home.

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*To be published.

It is the tumor most frequently encountered in the ovary and although it is not confined to any decade of life, it is usually seen when patients have passed the fourth decade. A cystic tumor that completely fills the abdomen of a child is most likely to be of this type. It is most often confused with the papillary cystadenoma which, under this classification, is designated as malignant and will be alluded to later. Since these cysts are usually large and benign, and are not infected, their removal is facilitated by evacuation of their content without fear of contamination of the peritoneal cavity. The prognosis always can be stated to be excellent.

Under benign neoplasms, in order of their importance, are classed endometrioma (endometriosis), fibroma, leiomyoma, and luteoma. Of this group endometriosis, which is closely allied to the tarry cyst, is the most common and the most important since it is encountered when patients are between twenty-five and thirty-five years of age and it has a decided tendency to destroy the reproductive function. The process is, of course, not confined to the ovary but in advanced cases will extend to the uterus and sigmoid colon. These structures may all be adherent in one mass, and if so the only treatment is surgical extirpation with castration. In some of the less involved conditions, and if one ovary is relatively free from the process, then conservative surgical treatment is in order, with a view to retaining the menstrual function if not the reproductive function. If patients have been fortunate enough to have a family before the disease becomes extensive, the latter function need not be given consideration.

Fibroma, leiomyoma, and luteoma are rare benign tumors and of little clinical interest. These are almost all encountered in women who have passed the menopause. Their presence is usually made known by their unusual weight and their removal is indicated.

MALIGNANT OVARIAN NEOPLASMS

Malignancies of the ovary have been studied by gynecologists and pathologists for a long time and many methods of grouping these tumors have been suggested. The classification here proposed (Table I) is not based so much on the histologic nature of the tumor as on the rate and manner of growth of the tumor and what it does to the patient. For example, some tumors grow slowly while others grow rapidly and recurrences are the rule. It is to be noted that the term "papillary" in this classification indicates malignancy. It is pathologically sound to regard and to treat as malignant any tumor which results in the formation of papillary epithelium, particularly if the growth tends to perforate the primary wall and to implant itself on adjacent structures. To do otherwise is to court disaster. Papillary epithelium behaves about the same wherever it is seen. If it appears in the urinary bladder it may or may

distress is secondary to the rupture and unless the physician is alert to these events, unnecessary operation may be advised. An appendicectomy has been mistakenly performed incident to the sequence of symptoms of rupture of a Graafian follicle cyst. When simple cysts do not rupture they may attain considerable size and may be easily discernible by bimanual examination. These cysts usually are not tender unless they are associated with secondary inflammation or torsion and they are either unilocular or multilocular. The majority of them are unilocular. If a simple cyst is judged to be more than 10 cm. in diameter, it is unlikely that it will disappear spontaneously. However, if there are no symptoms which require immediate surgical interference in cases of movable cysts it is safe to defer interference for two to three months, since these cysts, if patients are less than thirty-five years of age, are rarely neoplastic.

If a cyst is small, or if it is large, and is somewhat fixed under the broad ligaments or in the cul-de-sac, either a corpus lutein cyst or a benign dermoid cyst must be suspected. To distinguish between the two is not often possible clinically unless a roentgenogram reveals the presence of teeth or some calcium or bony deposit. The chocolate or fatty cysts of young women require most careful consideration. They are always benign but the interference with menstrual and reproductive functions may become irreparable. Surgical treatment must be instituted reasonably early, so that sufficient ovarian substance can be retained to influence the menstrual function if not the reproductive ability. Unfortunately this group of cysts is much larger than it is usually considered to be, and since the happiness of many women depends partly on their power of reproduction, these lesions, which have a decided tendency to destroy it, should receive more attention.

Benign dermoid cysts make up about 10 per cent of all cysts. They rarely produce symptoms unless they become secondarily infected or twisted. They are likely to become infected because of their sebaceous content and their close proximity to the sigmoid colon. A twisted ovarian dermoid rapidly becomes necrotic and then purulent, with the usual sequence of an acute pelvic inflammatory mass. Under such circumstances, surgical treatment is indicated at once. Great care is required during removal of these cysts to avoid rupture and secondary peritonitis. When they are not twisted or acutely inflamed, the gross appearance of their surface, which resembles frosted glass, easily distinguishes them from the usual unilocular, simple cyst.

BENIGN OVARIAN NEOPLASMS

The cystadenoma is the outstanding example of this group of neoplasms. The tumor arises in the substance of the ovary, in contradistinction to the simple follicular cyst. It can be unilocular but it is more frequently multilocular and contains a watery or mucoid material.

not be quiescent but if it is disregarded eventually it will kill the patient. The same can be applied to the ovary and it is for these reasons that the term "benign papillary cystadenoma" is not included here. If the tumor is papillary it is malignant and is so classified.

Papillary adenocarcinomata originate, as a rule, from the surface of the ovary and range from a low to a high grade of malignancy. Since they extend from the cortex of the ovary, they become attached early to adjacent structures and shortly they assume such proportions that they are regarded as inoperable. Ascites is the rule and metastasis to the omentum, bowel, and parietal peritoneum occurs within a few months. It is known that, given this type of malignancy, the prognosis is generally poor, but it is to be remembered that the secondary growths may become quiescent following removal of the primary tumor, followed by radium and Roentgen therapy. The longest duration of life following such a procedure, within our experience, if ascites and metastasis existed, was twenty years. There is a high incidence of bilateral involvement in these cases, so that if the papillary growth is still confined to the ovary, it is far safer to remove both adnexa and the uterus. Unless these patients are too greatly debilitated from the malignancy, they should be subjected to exploration and the question of operability determined.

Malignant ovarian cysts are designated "carcinomatous cystadenomata" and they compose one of the most important groups of tumors encountered in the pelvis. They are of interest because they are usually multilocular, and about 50 per cent are bilateral. The malignancy varies in grade but the majority are of Grade 1 or Grade 2. The malignant tissue remains confined within the cyst for long periods, which characteristic is in the patient's favor, since it is possible completely to remove the cystic tumor and cure the patient. When they perforate it is usually near the pedicle or at points of greatest pressure, so that care must be exercised during their removal. Cysts of low grade of malignancy may be filled with pseudomucin, but if the content is watery or bloody it is indicative of a more rapidly growing tumor. They are grouped as "papillary," "nonpapillary" or "mixed papillary and nonpapillary."

The solid carcinomata of the ovary represent a much smaller group but they also vary in rate of growth. There is a high incidence of pelvic attachment and extension to distant nodes. Ascites is a frequent finding and a bad one in relation to prognosis. These tumors are best studied separately from the cystic malignant growths and the papillary adenocarcinomata.

Carcinomatous dermoids occasionally are encountered; this makes it necessary to regard dermoids as malignant until they are proved to be benign. The consequence of a neglected malignant cyst of this nature is 100 per cent fatality because the carcinoma is usually an epithelioma of

TABLE I. ANATOMICOPATHOLOGIC CLASSIFICATION OF ADNEXAL CYSTS AND NEOPLASMS

I. Ovaries

A. Cysts

1. Inflammatory (subserosal)
2. Simple
 - a. Unilocular
 - b. Multilocular
3. Cysts of corpus luteum
4. Dermoid cysts (benign)

B. Neoplasms

1. Benign
 - a. Cystadenoma
 - (1) Unilocular
 - (2) Multilocular
 - b. Adenomyoma (endometriosis)
 - c. Fibroma
 - d. Leiomyoma (fibromyoma)
 - e. Luteoma
2. Malignant
 - a. Papillary adenocarcinoma
 - b. Carcinomatous cystadenoma
 - (1) Papillary
 - (2) Nonpapillary
 - (3) Mixed
 - c. Solid carcinoma
 - d. Carcinomatous dermoids
 - e. Luteoma
 - f. Teratoma
 - g. Sarcoma
 - h. Secondary carcinoma
3. Neoplasms of questionable nature
 - a. Granulosa cell tumor
 - b. Arrhenoblastoma

II. Parovarium

A. Cysts

1. Unilocular
2. Multilocular

B. Neoplasms

1. Leiomyoma

III. Fallopian tubes

A. Cysts

1. Hydatids of Morgagni

B. Neoplasms

1. Benign
 - a. Adenomyoma
2. Malignant
 - a. Adenocarcinoma
 - b. Squamous cell carcinoma
 - c. Secondary carcinoma
 - d. Sarcoma (rare)

is more common and can be a tumor of Krukenberg type or an extension from a fundal cancer or an ovarian papillary adenocarcinoma. Sarcoma of the tubes is extremely rare.

SUMMARY

The classification given herewith is on an anatomicopathologic basis. It is sufficiently descriptive and is not confusing. In dealing with ovarian cysts and neoplasms sufficient knowledge of their characteristics and behavior is necessary for appropriate treatment to be instituted.

THE TREATMENT OF HABITUAL ABORTION BY PROGESTERONE

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THE use of progesterone and progestin-containing extracts in the treatment of habitual abortion has a definite experimental background. The reader is referred to the works of Corner, and Corner and Allen¹⁻³ for historical and experimental data. Suffice it to say that the presence of the corpus luteum, active extracts of the tissue, or the chemically pure hormone itself is necessary for the maintenance of normal pregnancy in the rabbit. In the human being, the corpus luteum remains active up to the fourth month, when it begins to degenerate slowly, usually until about the sixth or seventh month, when there remains little or no evidence of its presence. Pratt⁴ has demonstrated that there is less than one international unit of progesterone in 40 gm. of human corpus luteum, and Bloch⁵ has shown that there is less than 1 unit in each of 8 and 12 liters of sow's blood. These observations probably mean that production and utilization of the hormone are continuous and that there is little storage. The amount used in the treatment of habitual abortion must of necessity be empirical until sufficient cases have been followed and further experimental work has been done.

Below are reported the results of treatment of eight cases of habitual abortion with progesterone or progestin-containing extracts. The general method of treatment followed was the intramuscular injection of progesterone, weekly, as soon as pregnancy was established up to, and including, the sixth lunar month of gestation. In each of the following cases, only the essentials are reported. In all patients the blood Wassermann was negative, and nothing could be elicited from the history, physical examination, or laboratory data which might account for the abortions, except in Case 6 where a Dudley operation had been performed. Two patients, Cases 4 and 8, had stigmata of an early pituitary failure.

high grade of malignancy. Attachment or perforation of the capsule stamps them as incurable. However, the opposite is true; that is, if they are unattached cure is almost sure to follow surgical removal.

A luteoma is a solid tumor which, although usually benign, occasionally grows locally and is productive of the condition designated as pseudopregnancy. The tissue is typically yellow and is not highly malignant. Complete removal always should be attempted.

Other solid malignant growths are teratomata, sarcomata, and secondary carcinomata. Histologic description here is unnecessary but the importance of early surgical treatment of these tumors should be stressed. Teratomata and sarcomata are highly malignant but usually curable, as they can be removed before extension to adjacent structures has taken place. Secondary carcinomata including Krukenberg's tumors represent metastatic growths on the surface of the ovary from other carcinomata, usually of the stomach, and are therefore inoperable. Discovery of bilateral ovarian tumors which are covered with a mucoid substance should at once lead to the suspicion of a Krukenberg tumor, and if the growth is of this nature further treatment is useless.

NEOPLASMS OF QUESTIONABLE NATURE

There is a group of tumors which probably arises from embryonic rests or indifferent cells in the substance or in the hilum of the ovary, the benignancy or malignancy of which is not definitely settled. Some, such as the arrhenoblastoma, produce a hormone which gives rise to masculine secondary sexual characteristics. Another more common tumor, which occurs after the menopause, is the granulosa cell tumor. Under its hormonal influence, periodic postmenopausal menses may occur. All symptoms subside following local removal of the tumors.

PAROVARIAN GROWTHS

Cysts which occur in the parovarium may be both unilocular and multilocular; malignancy in them is practically unknown. The only neoplasm to be considered is the leiomyoma and when it is seen it usually is in conjunction with uterine leiomyomata.

TUMORS OF THE FALLOPIAN TUBES

Hydatids of Morgagni frequently occur at the fimbriated ends of the Fallopian tubes, but are of little clinical or surgical significance. Neoplasms of the Fallopian tubes are both benign and malignant. The adenomyoma is the only benign lesion of importance and occurs as a rule together with generalized endometriosis, although independent adenomyomas are seen. If they produce pain excision is indicated.

Primary malignancies of the Fallopian tubes are rare. Adenocarcinoma and squamous cell carcinoma have been described. Secondary carcinoma

1937. One unit of progesterone was given weekly, beginning Apr. 7, 1936, up to and including June 29, 1936. During the early months of pregnancy, the uterus was retroverted, but spontaneously assumed the anterior position at about three months. A normal 3330 gm. female was delivered Nov. 8, 1937. A total of 10 units of the hormone was used.

CASE 6.—A twenty-eight-year-old para 0, gravida iv, who aborted in 1931, 119 days after the last menstrual period; again in 1933, 111 days after the last menstrual period; again in 1934, 112 days after the last menstrual period. The last menstrual period for the fourth pregnancy was Apr. 20, 1935. She was under the care of another physician who referred her for progesterone therapy. One international unit was given on July 18, three units on the twenty-second, 5 units on the twenty-seventh. On the twenty-ninth of July she complained of bearing-down pain but had no bleeding. Another unit was given on the twenty-ninth. Three units were given on August third and fifth, since she was nearing the time of her previous abortions. On August 9, she complained of a sensation of heaviness in the pelvis not unlike that experienced with her previous abortions. She was given $\frac{1}{4}$ gr. of morphine and five units of progesterone. On the tenth of August, she noted something bulging from the vulva but had experienced no pain. She was obviously aborting and was therefore hospitalized. A 17 cm. normal fetus and a 7 cm. placenta were delivered. Bleeding was profuse, necessitating packing. Examination showed that the cervix had a laceration extending from the external os through the internal os, on the posterior lip. This was obviously responsible for all the abortions within the neighborhood of 110 days. On the seventh day, the laceration was repaired and the patient advised to become pregnant again, which she has been reluctant to do. A total of 24 units of progesterone was used.

CASE 7.—A twenty-nine-year-old para 0, gravida iv, whose first pregnancy was a miscarriage at six months of a $2\frac{1}{2}$ -pound stillborn fetus. The second was at two months, and the third was an 800 gm. fetus at six months. The last menstrual period for the fourth pregnancy was Aug. 4, 1936, and the estimated date of confinement May 11, 1937. One international unit of progesterone was given weekly from Sept. 23, 1936, to Mar. 8, 1937. A 4150 gm. normal male child was delivered May 13, 1937. There was a 1,000 c.c. postpartum hemorrhage. Twenty-one units of the hormone were used.

CASE 8.—A thirty-four-year-old para 0, gravida v, who had had gonorrhea. In addition there was some evidence of anterior pituitary dyscrasia. The first pregnancy terminated at two months, the second was twins at three months; the third at three and one-half months, and the fourth at five months. The last menstrual period of the fifth pregnancy was Feb. 26, 1937. Beginning March 23, one unit of progesterone was given weekly. On May 15, there were spotting and dull backache. Five units of progesterone were given and $\frac{1}{4}$ gr. of morphine. The uterus at this time was the size of a three months' pregnancy, and the cervix was closed. Again on June 5, 1937, she had lower abdominal and back pain and was given 5 units of progesterone. Pregnancy was uneventful until July 9, 1937, when she began to pass fluid per vaginum, had a feeling of heaviness in the pelvis, but no pain or bleeding. Examination at this time showed the cervix 2 cm. dilated and membranes bulging. Labor pains started, membranes ruptured and a normal stillborn fetus was expelled July 11, 1937. It weighed 170 gm. and was 21 cm. long. The placenta and cord appeared normal. Examination after delivery showed no pelvic abnormality. A total of 25 Rb. U. were used.

Of the eight patients whose pregnancies have terminated, there are 2 failures, one which can be attributed to the Dudley operation (Case 6). The only abnormality so far as the fetus or placenta was concerned

CASE 1.—A thirty-seven-year-old para 0, gravida iv, whose first pregnancy terminated at seven months with a living female child weighing 3¼ pounds which died within a few hours. The second and third pregnancies terminated spontaneously at three and four months, respectively. The last menstrual period for the fourth pregnancy was Oct. 1, 1934, and the estimated date of confinement was July 8, 1935. Pregnancy was uneventful until Jan. 30, 1935, at which time the patient had cramps and bleeding. Morphine was given and bed rest instituted. Four international units of progesterone were given, and this amount continued every other day for ten days. No therapy was given for the next ten days, and then four international units of progesterone were given every other day for six doses. Early in March, the patient had slight spotting with cramps, and this occurred again in the latter part of March. Pregnancy was again uneventful until June 27, 1935, at which time there was some spotting. It is interesting to note that at the site of all injections, there occurred local allergic-like reactions which persisted for about two weeks after the last injection. The patient was delivered of a 3,150 gm. living, normal female child. A total of 44 international units of progesterone was used.

CASE 2.—A twenty-five-year-old para 0, gravida iv, whose first pregnancy ended in a spontaneous abortion at four months. The second ended in the third month and the third in the second month. Vitamin E was given during the second pregnancy without effect. The last menstrual period was Apr. 1, 1935, and the estimated date of confinement Jan. 7, 1936. Pregnancy was established by examination and ovulation test, and on May 14, 1935, 5 K.U. (1 international unit) of proluton¹ was given. On May 15 there was some bloody show but no cramps. This occurred again on June 15. One international unit of progesterone was given weekly until Nov. 8, 1935. The patient was delivered of a normal, full-term, female child, weighing 3,650 gm. Thirty-one units of the hormone were used.

CASE 3.—A thirty-two-year-old para 0, gravida iii, whose first pregnancy ended in a seven-month-premature child which was dead at birth. The second pregnancy terminated spontaneously at five months. This patient had obvious stigmata of pituitary failure which no doubt dated from the time of puberty. The menstrual cycle had always been very irregular and her build tended toward the masculine, with male distribution of pubic hair. On pelvic examination, there was a fibroid on the fundus about 4 cm. in diameter and one on the cervix about 3 cm. in diameter. One international unit of progesterone was given weekly from Oct. 10, 1936, to Jan. 21, 1937, a total of 14 units. On Nov. 23, 1936, the patient spotted for one day without pain. Pregnancy was otherwise uneventful. A 2960 gm. male child was delivered Apr. 8, 1937. The infant was very cyanotic and circumoral cyanosis persisted for seven days. The testes were small, and that on the left was undescended. X-ray showed a definitely enlarged thymus which was treated by the usual procedures. On discharge from the hospital and six weeks later the infant appeared normal. The placenta was about normal in size and grossly had a peculiar purplish gray sheen. Microscopically, it showed normal tissue.

CASE 4.—A twenty-nine-year-old para 0, gravida iv, who aborted at two months in 1933, at two months in 1934, and at four months in 1935. The last menstrual period for the present pregnancy was May 15, 1935. She was given one unit of progesterone from July 2 to October 7. A 3,480 gm. normal female was delivered Feb. 8, 1936. A total of 19 international units of the hormone was used.

CASE 5.—A twenty-nine-year-old para i, gravida v, whose first pregnancy terminated in a full-term delivery in 1926. The next two pregnancies terminated at four months and the fourth at six months. The last menstrual period for the fifth pregnancy was Feb. 19, 1936, and the estimated date of confinement was Nov. 26,

above, the small amounts necessary to relieve dysmenorrhea,¹⁰ and the large doses necessary to prepare a premenstrual endometrium in the human castrate (190 units).¹¹ No conclusion can be drawn from the series of cases presented and those cited from the literature as a proof that progesterone is effective. To do this, it will be necessary to have a very large series of cases so that the effect of the hormone can be evaluated statistically. Similar conclusions could be reached if in the same patient every other pregnancy should be treated with the hormone. No hormone therapy should be employed other than progesterone.

CONCLUSIONS

A series of eight cases of habitual abortion treated with progesterone are presented, to be considered with those already reported by the authors quoted. The patients in the cases presented were treated with from 10 to 44 international units of progesterone during the first six lunar months of pregnancy. No other form of endocrine therapy was used. There was one failure due to an operative laceration of the cervix, and one not as yet accounted for. Half of the patients had spotting, and one had spotting with cramps. All infants were apparently normal with the possible exception of Case 3. Smaller amounts of the hormone than one unit weekly may be sufficient to carry a pregnancy to term.

The author wishes to thank Schering Corporation for supplying part of the progesterone (proluton) used in this study.

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Costa, P. N., and Pastorini, R.: Generalized Peritonitis Complicating Electro-Coagulation of the Cervix, Bol. Soc. de obst. y ginec de Buenos Aires 2: 271, 1937.

The authors report two deaths following electrocoagulation of the cervix.

I. On the ninth day following the admission of a patient complaining of menstrual disturbance and some pain in the lower abdomen, after rest in bed and hot vaginal douches, electrocoagulation of the cervix was performed because of a chronic endocervicitis. A generalized peritonitis occurred. The patient died four days later. At autopsy the diagnosis was confirmed.

The second patient complained of metrorrhagia and menorrhagia. Diagnosis of chronic cervicitis was made. Electrocoagulation of cervix was done on May 24, 1937. On June 9, she was admitted to the hospital with abdominal pain and distention. She died on June 13, and the diagnosis of generalized peritonitis was confirmed at autopsy.

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was in Case 3. The amount of progesterone used varied from 10 to 44 international units in the individual cases. Four of the 8 patients had some bleeding, and one had bleeding with cramps. Obviously no hard and fast rule for treatment can be given from this small series of cases, but they are presented and reported with those of other investigators so that the effect of the hormone can better be evaluated.

Knab⁶ cites two cases treated with 2 K.E. of luteogan on two successive days. The patients up to the fourth month were apparently progressing satisfactorily. Beyond the fourth month observations are not reported. Sellheim⁷ treated 9 patients with serum of pregnant women by giving 10 c.c. every fourteen days. His results are reported as satisfactory. Krohn, Falls, and Lackner⁸ reported 8 cases of habitual abortion in a series with threatened abortion. Cases 5, 6, 9, 11, 12, 13, 16, and 19 were given one international unit of progesterone twice weekly until the thirty-second week. Kane⁹ reported 40 cases. Of these 40 patients, 20 had had one previous abortion, 14 had had 2, 4 had had 3, 1 had had 4, and 1 had had 6 previous abortions. Of the 40 patients, 10 had 1 living child each and then had aborted one to three times subsequently. Kane reported 4 failures. One pregnancy ended at six months. In another, a two-month fetus was expelled after five months' treatment, and there was 1 abortion at two, and 1 at three months. Kane treated his patients as follows: Proluton (progesterone) in 1/25 international units was given every other day for 10 doses. This was repeated at three-week intervals up to the thirty-second week. At the most, his patients received a total of 2 international units of the hormone. In addition to the hormone, each patient received 0.5 gr. of desiccated thyroid three times a day for four weeks, and 4 gr. of sodium iodide three times a day for two weeks following the thyroid medication. All medication was stopped at six months. In his series, Kane noted a definite increase in fetal abnormalities.

DISCUSSION

The causes of habitual abortion are many and varied, and the lack of the hormone produced by the corpus luteum is only one. Hypovitaminosis, hypothyroidism, defective decidual reaction, malformation of the ovum are a few of the causes other than chronic systemic disease. In his series, Kane⁹ reported the incidence of fetal malformations higher than normal, which indicated defective ova or defective decidual reaction. Perhaps some of these cases would have aborted if not treated. In some of the cases reported by the writer and other authors, some of the patients had had one full-term delivery followed by a series of abortions. All of these patients were treated successfully. One can only postulate that perhaps corpus luteum function was defective with succeeding pregnancies and that this state is liable to exist, just as one is subject to transient or permanent states of hypothyroidism.

The matter of dosage necessary to maintain pregnancy in the human being is at present empirical. The series reported by the author shows that from 10 to 44 units were successfully employed through six lunar months. Kane⁹ gave only a total of two units over a period of thirty-two weeks. Sellheim⁷ gave only 10 c.c. of serum from pregnant women every fourteen days with good results, and Krohn, Falls, and Lackner⁸ gave two units weekly from thirty-two weeks. The knowledge of the physiology of the ovarian hormones is not exact when one considers the amount used

ments were considered as not verified and were excluded from further consideration. This procedure gave 890 cases available for study. An attempt was made to interview the mother of each of the malformed children, the visits being made in the summer of 1934 by three fourth-year medical students. Since approximately 80 per cent of the births took place in hospitals, these institutions were visited, and pertinent facts were extracted from their records.

In about 25 per cent of instances, the defective individual exhibited *two or more* malformations. To simplify handling, each of these persons was assigned a *single diagnosis* which represented his most serious defect.

Definite information concerning the occurrence of placenta previa was secured for 741 of the pregnancies ending in the birth of malformed individuals. The chief defect diagnoses are summarized in Table I, according to body system; those involving primarily the

TABLE I

Incidence of placenta previa in association with pregnancies ending in the birth of children with defects. The chief defect diagnosis of each abnormal individual is classified according to its location. Note that only one case of placenta previa was observed in a total of 741 pregnancies.

BODY SYSTEM	DEFECTIVE CHILDREN	PLACENTA PREVIA
Nervous	480	1
Gastrointestinal	109	0
Bones, muscles, skin	78	0
Cardiovascular	59	0
Others	15	0
Total	741	1

nervous system are subclassified in Table II. Placenta previa occurred only once in the 741 pregnancies in which malformed children were born, this instance being associated with hydrocephalus.

TABLE II

Showing association of placenta previa with pregnancies ending in birth of individuals exhibiting defects involving primarily the central nervous system. Note seriousness of malformations.

DIAGNOSIS	DEFECTIVE CHILDREN	PLACENTA PREVIA
Hydrocephalus, spina bifida	305	1
Anencephalus	94	0
Craniorrhachischisis	22	0
Undescribed monsters	20	0
Meningocele	13	0
Microcephalus	10	0
Encephalocele	8	0
Others	8	0
Total	480	1

Placenta Previa in the Population-at-Large: Among 19 opinions from current textbooks in the English language, 7 give a frequency of one

THE COINCIDENCE OF PLACENTA PREVIA AND CONGENITAL MALFORMATIONS

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IN 1923, Greenhill¹ found references in the literature to 15 instances in which the birth of a congenitally malformed infant had been complicated by placenta previa; to this number, he added 6 cases from his own experience. These observations, together with a consideration of the theories dealing with the origin of placenta previa and congenital defects, led him to conclude: (1) "... that there is a not infrequent association between the two conditions," and (2) "... that the monsters associated with placenta previa are due to the faulty relation between the placenta and the fetus which gives rise to arrests in development."

No reports dealing with this association have appeared in the intervening years. This fact can be explained by the relative infrequency of the conditions as they occur independently of each other. Lack of such data, together with the opportunity afforded by my investigation of families possessing congenitally malformed children, prompted the writing of this report.

MATERIALS AND METHODS

Observations are presented upon: (A) The occurrence of placenta previa in a series of women bearing malformed children and (B) the birth of malformed children to a group of women suffering from placenta previa.

A. *Placenta Previa in Women Bearing Congenitally Malformed Children.*—The material forming the basis for this part of the study was secured in the following manner:

There were found in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and live born individuals who died in Philadelphia during the five years between Jan. 1, 1929, and Dec. 31, 1933. Each of these certificates was examined and the data on those noting the existence of any congenital defect were transcribed to duplicate official forms; 1,476 such certificates were located.

The deceased individual was considered to have possessed a defect under either of two conditions: (1) if the defect involved the surface of the body, or (2) if internal, its presence had been disclosed by operation or necropsy. Diagnoses not conforming to these require-

of placenta previa to each 400 cases of malformation, as compared with one case of placenta previa for each 1,000 of births in the general population, or for each 1,000 births of congenitally malformed. The difference in these two ratios might well be accounted for by the inaccuracies attendant upon the methods used in collecting the data, and also by the small amount of data available for analysis. The impression is gained from this study, that there is no unusual frequency of association between placenta previa and congenital malformation.

The absence of any statistically significant frequency of association between placenta previa and malformation lessens the possibility that there exists any causal relationship between them, as suggested by Greenhill. This fact is further strengthened by a study of the types of malformation found associated with placenta previa.

The diagnoses of malformations associated with placenta previa listed by the authors quoted in this report, combined with those found in the individuals reported here for the first time, are given in Table III. The first six diagnoses, marked with an asterisk, and representing

TABLE III

Showing combined figures for diagnoses of congenital malformations found to be associated with placenta previa: (a) as noted by other observers and (b) as recorded by the author.

MALFORMATION	NUMBER OF INDIVIDUALS
*Hydrocephalus	12
*Anencephalus	9
*Multiple	2
*Cleft palate	1
*Spina bifida	1
*Foot defect	1
Gastroschisis	2
<i>Holoacardius eumorphus</i>	1
Torticollis	1
Iniencephalus	1
Scleroderma	1
Encephalocele	1
Cyclops	1
Fetus papyraceous	1
Erythroblastosis	1
Total	36

*Defects known to duplicate in brothers and sisters.¹¹

26 out of a possible 36 individuals, are defects which I¹¹ have found to duplicate among brothers and sisters. This familial duplication suggests that these defects are the result of factors which operate prior to the time of fertilization. If a larger number of cases had been available for study, the remaining defects might also have been found to repeat.

SUMMARY AND CONCLUSIONS

The present data indicate that there is no unusual frequency of association between placenta previa and fetal malformation. This finding,

case in from 50 to 499 births, 10, one in from 500 to 1,000 births, and 2 give an incidence of one case in over 1,000 births. It is assumed that the above figures are based upon hospital statistics. J. Whitridge Williams² was under the impression that placenta previa occurs in private practice about once in every 1,000 births.

The method of locating cases of congenital malformation, i.e., from death certificates, would seem to make valid a comparison of their association with placenta previa, with the frequency of placenta previa in private practice, as given by Williams.

Although one case of placenta previa was observed in 741 pregnancies ending in the birth of malformed children, it is quite possible that no more cases would have been observed had a total of 1,000 such pregnancies been studied. On the basis of these figures, it appears that placenta previa occurred in pregnancies ending in the birth of malformed children with the same frequency as it is observed in ones which end in the birth of normally developed individuals.

B. Malformed Children Born to Women Having Placenta Previa.—The records of labors complicated by placenta previa, in 13 Philadelphia hospitals, were examined for evidence concerning malformation of the offspring. Of 433 such labors, 5 were associated with the birth of a malformed infant, or a ratio of 11 plus, per 1,000. This relationship is supported by reports from Genova,³ Lieberman,⁴ Kraul,⁵ Siegel,⁶ Kellogg⁷ and Walsh,⁸ comprising 1,264 cases of placenta previa, which included 18 instances of fetal malformation, or a ratio of 14 per 1,000.

Malformations in the Population-at-Large: Unpublished reports by Adair,⁹ and data which I¹⁰ collected indicate an incidence of approximately 5 fetal malformed individuals per 1,000 of births in the population-at-large.

DISCUSSION

The occurrence of 5 malformed individuals per 1,000 of all births, and of 11 per 1,000 of births complicated by placenta previa, suggests that some causal relation may exist between fetal malformation and placenta previa. These figures may express a relationship which is more apparent than real. For example: On the basis that 1 case of placenta previa occurs in each 1,000 births (Williams), the 433 instances of placenta previa births located in Philadelphia hospitals represent approximately 433,000 births in the population-at-large. In the latter number, there would be expected approximately 2,165 malformed offspring, based on a frequency of 5 per 1,000 births (Adair, Murphy). In this number, then, would have occurred the 5 cases of placenta previa associated with malformation found in the Philadelphia hospitals. The ratio of these 5 cases to 2,165 would be that of one case

turbance. Parrot and later Kaufmann suspected a congenital malnutrition of the cartilage cells. DeBück and Mayet,⁹ in 1900, advanced the hereditary theory, and believed that the cartilage cells underwent a process of degeneration. Virchow and Grawitz thought that these were cretins due to thyroid dysfunction. Durante¹⁶ in 1900 reported a case from a syphilitic mother. Cestan and Reignault⁷ attributed it to intrauterine rickets. Jansen,¹⁰ in 1912, propounded the theory that these dwarfs were due to changes in the fetus taking place in utero between the third and sixth week, when infolding occurs. At this time he states, "the flexible scleroblastomatous skeleton begins its changes into cartilage, and is very vulnerable to changes." If the amnion is too small, due to a retardation in its growth, then there is "the direct amniotic pressure infolding the embryo, and the indirect or hydrostatic pressure in the amniotic fluid, are enhanced." Due to this, there is considerable resistance to the circulation of the blood in the amniotic sac with resulting ischemia and hunger to the fetus, and Jansen goes on to say "that the glutton among the tissues is the cartilage, and it is first and most doomed to dwarfism."

According to Crew,⁸ this is an hereditary disease. For his experimental work, he has used the Dexter, a breed of the smallest cattle in Great Britain. He showed that the "Bulldog calf," which is an abortion product of the Dexter, resembles the human achondroplastic. The histologic appearance of the shaft and epiphysis of the bones of the achondroplastic dwarf is exactly identical with that of the "Bulldog calf." He believes that the incidence of these calves is based upon a simple Mendelian dominant character, and if such individuals were mated, about 75 per cent of the offspring would be "Bulldog calves." He also suspects a malformation of the pituitary gland during the second and third month of intrauterine life as the primary cause, with resultant interference in the process of cartilage and bone formation. Crew concludes that the severity of the achondroplasia depends on the degree of malformation of the pituitary.

Keith¹² found the pituitary gland to be very small in these dwarfs. Mesz, Fliederbaum and Markieszewicz¹⁴ thought this a syndrome of anterior lobe origin. Wheeldon²⁴ in 1920 published an excellent paper on "Achondroplasia." He agrees with Jansen's theory and believes that due to the too small amnion the "head curve must needs push the region of the visceral arches and the future face against the organs of the future chest and the chest wall." In this way he explains the flattening and depression at the base of the nose and the displacement of the hard palate toward the base of the skull.

Bangson² reported chondrodystrophia fetalis through five generations and produced an interesting chart of the family tree, which proved their adherence to the Mendelian theory. Warner²³ reports a case of homologous twins in which only one is an achondroplastic and the other twin entirely normal. This seems to contradict the Mendelian law since the hereditary theory holds for homologous twins. Royer¹⁸ believes that one must consider that the etiologic factor may be due to an absence of "growth impulse." Pritchard¹⁷ reported a three-and-one-half-year-old twin that was an achondroplastic dwarf and had been treated for rickets. The other twin was perfectly normal. He believes that the etiology is based on some dominant character in the germ plasm which leads to chondrodystrophic variation connected with some defect in the endocrine hegemony. Bauer³ reported a case of unilateral achondroplasia.

REPORT OF TWO CASES

The following two cases about to be described were the only children born from these parents, and their births were separated by an interval of only one year.

together with a consideration of the types of malformation found in association with placenta previa, leads to the conclusion that the one condition is in no way responsible for the occurrence of the other.

The author is indebted to Dr. Carl Bachman for criticisms and suggestions.

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ACHONDROPLASIA FETALIS

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THROUGHOUT the records of ancient history one can find evidence of the existence of dwarfs. Many references are made to them in the mythologic writings of Greece. Due to their small stature, shortened limbs, and apparently normal intelligence, they were very popular with the nobles of ancient Rome who had one or more dwarfs in their retinue to serve them. Rurak²⁰ reports an eighth century basrelief of an achondroplastic dwarf which was obtained from one of the temples of Amurâdhapura, in the island of Ceylon. They were not uncommon in this region and were worshiped as the god Bes, who ruled over the realm of sexual intercourse, childbirth, art, singing, and dancing. The Egyptians also set up among their many gods one called Ptah, a typical example of chondrodystrophiananism. Many of the ancient masters incorporated them in their paintings. Catherine de Medici and Empress Ann of Russia endeavored to establish a race of achondroplastic dwarfs by intermarriage, but were unsuccessful. This was due to the pelvic deformity present in the majority of these dwarfs, and the offspring could only be born by cesarean section. Today a race of dwarfs might certainly be a possibility.

Although it has been indisputably established that these achondroplastic dwarfs existed during ancient times, it was not until 1878 that Parrot¹⁵ established them as a definite clinical entity and gave them the name of "achondroplasia." Rhomborg, previously in 1817, had described a human fetus with short limbs. Virchow, in 1856, attributed these cases to rickets and this added to the confusion. Parrot's description of achondroplasia was later confirmed by Porak and Durante in 1891.¹⁶ In 1893, Kaufmann¹¹ gave it the name of "chondrodystrophia fetalis," because there is "a malnutrition of the cartilage rather than an absence of the cartilage."

The etiology has not been definitely established. Various theories have been advanced. Bohn and Schwab⁴ in 1868 believed it to be due to a placental dis-

In both these cases, the chest cavity was much narrower than normally found, and in compressing the chest there was very little elasticity. The photographs of M(2) showed the pyramidal shape and constriction of the thorax. Jansen noted "that the chest was often shortened and consequently was too small for the proper accommodation of the vital organs. The caudal circumference was pressed inward so that the sternum was directed almost horizontally and its shape came to resemble a calotte." The mammae in M(2) were found to be located far out on the thorax just along the axilla and below the clavicle. The trunk in these cases may be longer than normally found. The musculature was extremely well developed. A very characteristic finding was the shortening and thickening of the limbs. Due to the micromelia, the nanus resembled the earlier fetal conditions since the limbs were short in relation to the trunk. This shortening was more marked in the proximal part than in the distal. The limbs were curved with the convexity curved outward. In these two cases the vertebral column was not shortened, nor was there any dorsolumbar kyphos. This had been reported, and sometimes the vertebrae might be wedge-shaped. The buttocks and abdomen were prominent. The pelvis was small in relation to the rest of the body.

The hands were thick and small and the fingers were stubby. The fingers reached to the anterior superior spines. The second and third metacarpals formed an angle of about 40 degrees with one another instead of the usual 32 degrees, giving rise to the "main en trident." The feet were rotated outward. Other stigmata have been reported such as harelip, narrowed foramen magnum, umbilical hernia, etc. It is said that their sexual appetite is often enhanced.

A study of the skeleton of Baby M(2) reveals many interesting points. The head was brachycephalic, being broad, short and very long compared to the rest of the body. The sella turcica was reduced in size. The fontanels and sutures were widely open. The parietal and frontal bosses were prominent. The squamous part of the occipital bone and the nasal bone were shortened. This accounted for the depression at the root of the nose. The bridge of the nose was flattened and sunken. The cervical vertebrae were well formed. The clavicles were extremely long, measuring $4\frac{1}{2}$ cm. in length, and ossification was more advanced than normally.

The thorax was elongated, narrow, and practically incompressible and inelastic. This was probably due to the extreme ossification of the ribs. The rib cartilage was heavy, thick, and shortened. There was some broadening of the ribs in their distal ends. Both the transverse and the anteroposterior diameters of the thorax measured less than normal. In the superior mediastinum, the bodies of the thoracic vertebrae were separated from the anterior chest wall by only 4 mm. At the caudal end, the distance between the xiphoid process and the thoracic vertebrae measured 13 mm. The lungs caged in this small thorax with the heart and thymus were able to expand only to a very small degree. The central point of the skeleton was not the symphysis as is normally the case, but was now the xiphoid process. There did not seem to be any abnormality in the spinal curvature, and the vertebrae were well developed. There was a generalized shortening and broadening of the long bones of the body. The humerus measured the same length as the ulna, and the radius was 1 mm. longer than the humerus. The femur was much shortened and was only 2 mm. longer than the tibia. The pelvis was small and funnel shaped. The pelvic cavity was narrow and the ossification appeared to be farther advanced than is normally found.

Russell²¹ found that histologically the long bones showed numerous transverse without development of the longitudinal trabeculae. Instead of the normal process of calcification occurring in the cartilaginous matrix, this is replaced by mucoid degeneration. There is swelling of the cartilage cells with disturbed nutrition resulting in mucoid degeneration. Later there is a transposition of the solid matrix into a fluid consistency. This gives rise to the dis-

Mrs. B. M. (Case 68680), aged eighteen years, married two years, menstrual history normal. Husband weighed 168 pounds, height 5 feet 7¼ inches. Family history: Patient's father was a very small man with a high chest. Had two normal uncles. Husband's father was also a small man. Husband's uncle was born a hunchback and died when eighteen years of age from pneumonia. Patient's long bones were normal, and measurements good. She weighed 141 pounds. Her prenatal course was uneventful. Patient entered General Hospital June 4, 1935, at 11:30 p.m. and a baby girl M(1) (Case 68684), was delivered in head presentation after a normal labor ending at 6:40 a.m. A faint fetal heart was elicited. Despite stimulants and artificial respiration, the baby died ten minutes after birth. Mother was discharged from the hospital in good condition.

External characteristics of Baby M(1) revealed large prominent frontal bones, a very narrow thorax, and short stubby extremities. Postmortem showed an achondroplastic dwarf with thickened and very small chest. The lungs were compressed and lying in a deep groove in the chest cavity. The lungs floated when immersed in water. The liver was very large and filled a greater portion of the abdominal cavity. The cause of death was due to maldevelopment characterized by a very small chest cavity, the collapsed lungs, heart, and thymus filling the lung cavity and leaving no room for the lungs to expand. Final diagnosis was "Achondroplastic dwarf with very small chest cavity. Atelectasis of the lungs."

Mrs. B. M. again became pregnant and was due to deliver in June, 1936, just one year after Baby M(1) had been born. Prenatal course was normal. Wassermann and Kahn tests were negative. Cephalic presentation. After a normal labor of twelve hours and forty minutes Baby M(2) (Case 60678) was delivered at St. Luke's Hospital at 4:32 p.m. on June 27, 1936. The baby was breathing about five times a minute with CO₂ and oxygen. Injection of alpha lobelin, warm bath, mouth to mouth breathing all failed and Baby M(2) died at 5:10 p.m.

Baby M(2) was an achondroplastic dwarf, well nourished, with pink thick skin and weighing 6 pounds 10 ounces. The face was round and flat with a cretin-like expression. The extremities were short and heavy. The hands and feet were fat and stubby. X-ray revealed both lung fields were atelectatic. Autopsy showed a very small thorax. The lungs were elongated and placed nearly entirely behind the diaphragm. Crepitation revealed a small amount of air in the alveoli. Both lungs weighed 19 gm. The liver was enlarged. Histologic examination revealed no abnormalities. Final diagnosis was "Achondroplastic dwarf with extreme deformity in the thorax. Amniotic aspiration."

DISCUSSION

There seems to be some confusion in the literature since one finds this entity confused with osteogenesis imperfecta, rickets, chondritis fetalis, dystrophie osseuse famialiele, etc., but the typical achondroplastic dwarf is easily recognizable at birth. Both Babies M(1) and M(2) were characteristic types of chondrodystrophia fetalis, and presented well-defined external characteristics which were mainly as follows:

The head was larger than usual and the circumference was greatly increased. The forehead bulged and the parietal eminences were accenuated, but this was not due to hydrocephalus. The fontanels were tense and bulging, and the sutures were widely separated. There was a depression and flattening of the bridge of the nose, giving it a pug nose appearance. The neck was short and thick and the head appeared to be set directly on the shoulders. The skin was thick, wrinkled and folded over the joints, especially that covering the arm and posterior part of the buttocks.

VITAMIN B₁ DEFICIENCY AS AN ETIOLOGIC FACTOR IN PREGNANCY TOXEMIAS*

PRELIMINARY COMMUNICATION

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AT THE present time the cause of preeclampsia and eclampsia is not known. Most of the investigations¹ in this field have revealed the results and not the causes of toxemia. Titus² has found a disturbed carbohydrate metabolism, Bartholomew^{3, 4} has studied placental infarcts, Hofbauer⁵ has found evidence of increased activity of the pituitary body, while Zangemeister,⁶ Plass,^{7, 8} Harding and Van Wyck⁹ investigated the problem of water retention. But no one has offered an adequate answer to the question: What exciting factor starts the chain of events that have been observed? A new approach to this problem is worthy of consideration.

It is to be emphasized that to find this causative factor it is necessary to search for it early in pregnancy or just when the signs of toxemia first appear, because the convulsive climax of eclampsia represents the final result of a profound disturbance.

In this preliminary communication the suggestion is offered: (1) That the pituitary body, anterior and posterior lobes, requires vitamin B₁ for its normal function. (2) That deficiency of this vitamin in the nonpregnant female causes hypofunction of the pituitary body which in turn causes the syndrome called beriberi. (3) Furthermore it is suggested that a deficiency of this vitamin B₁ during pregnancy causes a hyperfunction of the pituitary body which in turn gives rise to the manifestations of toxemia. This new concept harmonizes the findings of practically all investigators, and it may elucidate the cause of such unsolved problems as amenorrhea, hypoplasia of the uterus, hypertension, nondiabetic glycosuria, and other disorders possibly wrought through the action of the pituitary body.

During several years of practice in Canton, China, the author was impressed by the large number of patients who showed signs of clinical hypopituitary characteristics. In that same community the most common deficiency disease was beriberi or vitamin B₁ deficiency.¹⁰ Furthermore the incidence of the toxemias of late pregnancy was high.¹¹ These observations stimulated the comparisons which are given in Table I, and circumstantial support is found for the new concept of the cause of toxemia as stated above.

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turbance in the epiphysis. The muroid material is later absorbed. In some areas, calcification proceeds with resulting numerous irregular centers of calcification instead of a single center of ossification.

The changes which give rise to the characteristics of the chondrodystrophia fetalis are quite definite and were first outlined by Parrot. There is a retardation of the cartilage formation which takes place about the third week of fetal intra-uterine life, and an arresting of bone formation in the cartilage. There is a premature closing of the epiphyseal centers. The long bones, especially the humerus, and femur are mainly affected, and show marked shortening and thickening. The ulna and tibia do not show as marked changes, and these occur only where bone is replacing cartilage. Due to the excessive growth of the epiphysis, the ends of the bones have a mushroom appearance. This is due to the diaphysis, near the epiphysis, becoming cup shaped without producing any disturbance in the epiphyseal line. The flat bones derived from the membranes are not affected. The large head and bulging forehead, according to Janset, are due to a shortening of the distance of the pituitary fossa from the frontoethmoid junction and a premature tribasilar synostosis resulting in a shortening of the skull and its base and finally a depressed nasal bridge.

CONCLUSION

1. The authors present these cases as an interesting phenomenon, the occurrence of two consecutive pregnancies resulting in chondrodystrophia fetalis.

2. This is possibly further confirmatory evidence of an hereditary basis in this condition.

3. It is interesting that, in both cases, death was apparently due to the same cause; a constricted thorax and deficient chest capacity.

4. Typical cases of achondroplasia fetalis present certain well-defined characteristics which are easily recognizable at birth and should not be confused with other clinical entities.

5. An apology for the failure to study the size of the pituitary gland may be in order.

The writers wish to express their appreciation of the work of Mr. Donald Meyer, Kansas University medical student, in preparing and mounting the skeleton of Baby M(2). They wish, also, to express their appreciation for the advice and direction of Dr. Ferdinand C. Helwig, Pathologist, St. Luke's Hospital, Kansas City, Mo.

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period for six months, and she had had no symptoms of cramps or soreness in the breasts. The patient was given intramuscular injections of vitamin B₁, 6.6 mg., every other day for seven doses. The day following the last injection she developed mild cramps and had a menstrual flow amounting to a large spot on the pad.

If the lack of vitamin B₁ is a fundamental cause of hypofunction of the pituitary body as mentioned above, then one would expect to find in beriberi a depression of all of the functions of this master gland and such seems to be the case. It is not necessary to discuss here the many different functions of the pituitary nor to separate the actions of the different lobes. For simplicity only five functions are given as a basis of comparison. The normal pituitary body acts as follows: (1) Insulin production is stimulated by action on the pancreas. (2) Water metabolism is regulated through the kidney. (3) Blood pressure and capillary tone are affected. (4) Gastric secretions are inhibited. (5) The ovarian follicles and corpus luteum are stimulated. Now in vitamin B₁ deficiency,¹⁴ such as is seen in beriberi, hypofunction of the pituitary might be indicated by such findings as: (1) hyperglycemia, (2) edema, (3) low blood pressure, (4) loss of appetite and atony of the gastrointestinal tract, (5) atrophy of the ovaries with failure of ovulation. Furthermore in vitamin B deficiency in test animals, the pituitary body and the adrenals are enlarged, and this increase in size may be a compensatory hypertrophy resulting from a lack of vitamin B₁.

Whereas vitamin B₁ deficiency seems to give rise to hypofunction of the pituitary body in the nonpregnant patient, a similar deficiency during pregnancy may cause a hyperfunction of the pituitary which in turn produces the syndrome of eclampsia and preeclampsia. Evidence of hyperfunction of the pituitary body in pregnancy toxemias is shown by such findings as: (1) Disturbed carbohydrate metabolism, (2) edema, (3) elevated blood pressure, (4) nausea and vomiting, (5) prolan^{15, 16} in the blood and urine is high and the estrin is low. Furthermore Cushing^{17, 18} has found a basophilic invasion of the posterior lobe of the pituitary body, and he advances evidence that the degree of this basophilia represents a measure of neurohypophysial activation. In view of the toxic symptoms of preeclampsia and eclampsia, the term pituitary toxicosis might be used just as thyrotoxicosis is used to connote hyperthyroidism. The author suggests that vitamin B₁ is necessary for normal pituitary function just as iodine is necessary for the thyroid function. Thus the enlarged pituitary body as seen in vitamin B₁ deficiency would correspond to the enlarged thyroid gland (colloid goiter) due to iodine deficiency. Also as an adequate supply of iodine prevents colloid goiter, and furthermore can allay the toxic symptoms of hyperthyroidism, just so may sufficient vitamin B₁ prevent the enlargement and underfunctioning of the pituitary in the nonpregnant

TABLE I. PITUITARY FUNCTION IN PREGNANCY, PREECLAMPSIA, BERIBERI

	SIZE OF GLAND	CARBOHY- DRATE ME- TABOLISM	WATER METABO- LISM	BLOOD PRESSURE	GASTROIN- TESTINAL TRACT	EFFECT ON OVARIES
Normal pitu- itary ¹²	Normal	Stimulates insulin pro- duction	Regulates through kidney	Affects B. P. and capillary tone	Inhibits gastric secretion	Stimulates follicles and corpus luteum
Normal preg- nancy. Phys- iologic hyper- function of pituitary	Enlarged	Low sugar tolerance	Normal	Normal	Early nausea	Late months. Prolan low. Estrin high
Preeclampsia. Pathologic hyperfunc- tion of pitu- itary	Enlarged	Hypo- glycemia	Edema	Elevated B.P.	Nausea, vomiting	Late months. Prolan high. Estrin low
Vitamin B ₁ de- ficiency. Beriberi. Possible hy- pofunction of pituitary	Enlarged	Hyper- glycemia	Edema	Lowered B.P.	Loss of appetite. Atony of gastroin- testinal tract	Ovaries at- rophy. Failure of ovulation

Table I indicates that the major functions of the pituitary body are probably disturbed both in the toxemias of pregnancy and beriberi or vitamin B₁ deficiency. If vitamin B₁ is essential for the normal function of the pituitary body as suggested above, then the need for this vitamin should parallel the activity of the gland. Such is the case because the pituitary body shows increased activity during growth, puberty, pregnancy, and lactation, and at exactly these periods there is an increased requirement for vitamin B₁.¹³ Thus it would be logical to treat hypopituitary disturbances with vitamin B₁ and several cases with menstrual irregularities have been submitted to injections of crystalline vitamin B₁.

One case of interest is Miss H., student, nineteen years of age, who started to menstruate at the age of twelve and one-half years. The periods were irregular, but once a month, with diminished amount of flow until 1936 when there was only spotting for about one hour. Since the age of fifteen, the patient had frequent small nasal hemorrhages just before and during her menstrual period. In September, 1936, the patient was given repeated injections of theelin together with dicalcium phosphate and iron. The period increased to twelve hours' scanty flow, but the nasal bleeding continued. Then all medication was stopped and 500 units of crystalline vitamin B₁ was injected every other day for five injections, with the result that amount of flow definitely increased and for the first time during the school year there was no nasal bleeding.

Another case illustrates a possible relationship of vitamin B₁ to the menstrual function through the pituitary body. Miss C., 19 years of age, started to menstruate at 14.5 years. Her periods were irregular, once in one or two months. The flow was copious with moderately severe cramps during the week previous to the onset of her period. At the time of examination the patient had had no menstrual

tion demands more vitamin B₁, so that a relative lack could arise and this again produce changes leading to frequent toxemia. (3) Toxemia is more prevalent among the poorer patients, because their supply of vitamin B₁ may be scarcely enough for the nonpregnant state and the increased demands for this vitamin during pregnancy are not met and toxemia results. Prenatal care with the usual attention to diet increases the intake of vitamin B₁ and thus toxemia is prevented. The poor patient cannot afford fresh fruit and vegetables in the winter months when the prices rise, so the intake of vitamin B₁ is relatively less and toxemia in pregnancy increases. (4) Delivery often relieves the symptoms of toxemia because the demand for hyperfunction of the pituitary body, with its demand for more vitamin B₁, is taken away and the amount of vitamin B₁ available more nearly meets the needs for normal pituitary function. Vitamin B₁ is stored in the body only to a limited extent, so that a constant supply is necessary if a deficiency is to be avoided.

The practical application of the foregoing hypothesis is now possible with the availability of crystalline vitamin B₁²¹ for parenteral administration. Studies are now under way at Maternity Hospital, Cleveland, under Dr. Sidney Stone; and Pittsburgh, under Dr. Paul Titus; in Philadelphia by Dr. Clifford B. Lull and Dr. Philip F. Williams; in Chicago by Dr. D. S. Hillis, and in Atlanta by Dr. R. A. Bartholomew. It is hoped that further interest and cooperation will be stimulated.

SUMMARY

A new approach to the problem of the cause of preeclampsia and eclampsia is presented based on the suggestion that:

1. The normal function of the pituitary body is possible only when an adequate supply of vitamin B₁ is available.
2. Vitamin B₁ may be necessary for the pituitary as iodine is for the thyroid gland.
3. In the nonpregnant female a deficiency of vitamin B₁ leads to beriberi, the symptoms of which are produced by hypofunction of the pituitary body. The symptoms of beriberi include disturbed carbohydrate metabolism, edema, low blood pressure, atrophy of the ovaries, atony of the gastrointestinal tract.
4. In the pregnant female, this deficiency of vitamin B₁ results in overcompensation or malignant hyperfunction of the pituitary body thus producing the symptoms of toxemia, for example, disturbed carbohydrate metabolism, edema, elevated blood pressure, nausea and vomiting, increase in prolactin and decrease in estrin in the blood.
5. An adequate and constant supply of vitamin B₁ should prevent toxemia and perhaps cure it.
6. This new concept harmonizes for the first time practically all of the conflicting findings and confusing manifestations of toxemia.

patient on the one hand, while on the other hand this same vitamin may allay the symptoms of malignant hyperactivity of this gland as seen in the toxemias of pregnancy.

With the onset of pregnancy, the pituitary body enlarges and meets the increased demands with increased function. It is suggested here that this increase in function can proceed normally only if there is an adequate increased supply of vitamin B₁. During pregnancy the requirement for vitamin B₁ is increased 3 to 5 times. Therefore, if the expectant mother does not increase her intake of this vitamin accordingly, she may unwittingly forge the first link in the chain that may bind her fast to a later toxemia. Thus the cause of toxemia probably operates early in pregnancy and is not to be found at the time of an eclamptic convulsion. It may seem paradoxical to suggest that a deficiency of vitamin B₁ in the nonpregnant female causes hypopituitarism, while in the pregnant patient that same deficiency causes a hyperfunction of the same gland. However, it may be that the onset of pregnancy produces such changes in the maternal organism that the pituitary body not only compensates for a lack of vitamin B₁ but actually overcompensates to the detriment of the patient. Why then do beriberi and neuritis occur in the pregnant state?^{19, 20} Why do not these manifestations of vitamin B₁ deficiency always give rise to preeclampsia and eclampsia? It is possible that a deficiency of vitamin B₁, which is present for some time before the onset of pregnancy, may so impair the function of the pituitary body that the additional burden of a gestation makes the vitamin deficiency so severe that the gland is unable to compensate, and neuritis and beriberi result just as in the nonpregnant patient. If the deficiency of this vitamin occurs only after onset of pregnancy, then the pituitary seems capable of overcompensating, thus producing a toxemia.

In searching for the fundamental etiologic agent in the pregnancy toxemias, the following questions must be answered. Why is toxemia more common in: (1) primiparae, (2) multiple pregnancies and hydatid mole, (3) among the poorer patients, (4) and why does toxemia so often disappear after delivery of the fetus? The new concept offered in this report gives a probable explanation for all of the questions raised above: (1) the pituitary body of the primipara is smaller than that of the multipara, so that the glands adjustment to insufficient vitamin B₁ in the organism is likely more difficult and limited and thus toxemia makes its appearance more frequently in such cases. (2) In multiple pregnancies the requirement for vitamin B₁ is increased still more than the usual increased demand for a single pregnancy, so that the mother is likely to take a relatively insufficient amount of this vitamin, thus causing toxemia more frequently. In the case of hydatid mole, the rapid cellular growth is brought about perhaps by the hyperfunction of the pituitary body, and this hyperfunc-

EMBRYOLOGIC CONSIDERATIONS

In the embryonal growth of the gonad, unused mesenchymal germinal cells may remain because of developmental errors. These cell rests may later proliferate and manifest themselves in several ways.

a. If the rests are misplaced very early, at the time of asexual embryonal growth of the gonad when the mesenchyme is undifferentiated, undetermined and neutral, they may later give rise to tumors of ovary, testis or hermaphroditic gonad. These embryonal relics retain all their fetal qualities, i.e., the proliferative potencies and the asexual neutral character. These germinal cells are neither male nor female nor hermaphroditic, but are pathologically neutrally determined mesenchymal cells which are embryonally undifferentiated, inferior, disgerminal, hence disgerminomas.

In the further development of the gonad differentiation of the mesenchyme occurs² either (1) in the male direction into "Sertoli cells" influenced chromosomatically and by the invading spermatogonia; (2) in the female direction into "granulosa cells" influenced chromosomatically and by the invading ovula.

b. If at this period by some process of malformation mesenchymal rests determined in the male direction are formed in the parenchyma of a gonad otherwise determined in the female line, then these may later arise in the ovary with prospective potentialities to form germinal cords or testicular channels. These cells are masculinizing in their effect and hence are called arrhenoblastomas.

c. Mesenchymal cell rests of female determination may be left in a gonad maturing in the female direction. These rests may then give rise to neoplasms of the ovary in which the cells follow their original inherent tendencies and hence develop into granulosa cell tumors.

The foregoing embryologic considerations conform with the views held by Meyer, Fischel, Schiller in Europe, Novak and Gray³ in America. They have been slightly modified from the stand taken by these authors in order to explain more readily the unusual incidence and clinical features of the neoplasm under discussion.

RELATIONSHIP BETWEEN DISGERMINOMA OVARIUM AND SEMINOMA TESTIS

The disgerminoma differs from the other growths in its congeneric group, i.e., the granulosa cell tumors and the arrhenoblastomas in that it occurs in both the female and male gonads. Its occurrence in the testis was described in 1898 by Chevassu who called this tumor a "seminoma." Some thirteen years later tumors of similar stamp occurring in the ovary were noted by Chenot⁴ who labelled them "seminoma ovarii." However, since the tumors do not masculinize the female nor effeminize the male, nor hyperfeminize or hypermasculinize, it is evident they are neutral. Robert Meyer after studying a series of these cases in the female rejected the term seminoma because they did not masculinize. The error in designating these tumors of the testis as seminomas arose through faulty interpretation of the histologic findings. The seminiferous tubules present in sections of so-called seminomas of the testes are not the product of the tumor, but merely mute evidence of the normal tissue structures overrun by large protoplasmic-rich neoplastic cells thought to be spermatoblasts.

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DISGERMINOMA OVARII*

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INTRODUCTION

THE ovary, because of errors in its embryologic development, is frequently the seat of rests, the potentialities of which are great and varied. If indeed the ovary has been compared to the fertile garden wherein bloom the rarest of growths, then too it has equally proved a jousting ground. Here the variant views as to the histogenesis of these very neoplasms forever clash, one gaining fleeting preeminence over the other. The variant tumors have truly been the enigma of both gynecologist and pathologist for their nature and origin have been the occasion of endless and bitter discussion. The *bête noire*, particularly of this group, is the disgerminoma. Until recent years it has been the source of considerable confusion. This has been due, not so much to failure of recognition, for its morphologic characteristics are comparatively uniform, but rather to the profusion of names to designate one and the same neoplasm. It appears that the "seminome" of the French, the "grosszellige karcinom" of the Germans and the many tumors described by English, American, and other authors as round cell sarcoma; embryonal, alveolar cell and solid carcinoma, mesothelioma, endothelioma, etc., fall into the category termed by Robert Meyer¹ as disgerminomas.

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REPORT OF CASES

CASE 1.—A well-developed and nourished negress, aged thirty-four, and mother of two children, entered the University Hospital Apr. 10, 1923, complaining of pain and fullness in the lower abdomen. She gave a history of gradual enlargement of the abdomen for the past year. About the same time she noted a change in her menses from a regular and normal flow to a very painful and scanty catamenia. For



Fig. 3.—Case 1. Showing the cordlike arrangement of the cells and the scantiness of the stroma.

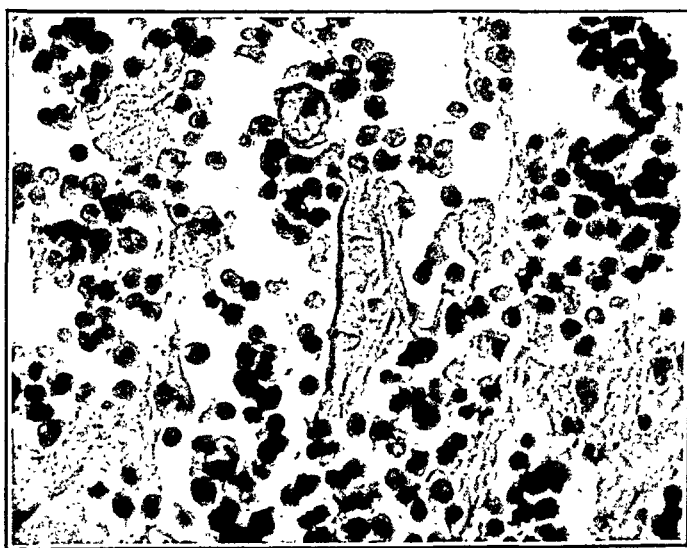


Fig. 4.—Case 1. Showing the cells with large hyperchromatic vesicular nuclei and scanty cytoplasm lying loosely apart and unsupported by a connective tissue framework.

two weeks prior to her admission she experienced fever and night sweats. Physical examination revealed an irregularly distended abdomen. Palpable through the abdominal wall was a large irregular mass which filled the abdomen up to the costal notch. Pelvic examination disclosed a parous outlet, a serosanguineous discharge from a lacerated cervical os, and a very small uterus behind the pubic arch.

Pathologic Report.—(a) Solid ovarian carcinoma (reclassified dysgerminoma).
(b) Hyperinvolution of uterus.

The origin of these growths is from early undifferentiated germinal cells in the embryonal gonad which never attained a specific power to sex direction. Therefore identical disgerminal pathologic structures may develop in both types of sex glands. For this very reason the term disgerminoma should be employed. It is descriptive and serves to indi-



Fig. 1.—Case 1. Showing the lobulated appearance of the tumor. Note the small involuted uterus.



Fig. 2.—Case 1. Showing the alveolar arrangement and distribution of cells, as well as the loose edematous stroma.

cate its origin as well as its place in the lineal scale of related tumors arising from germinal cell rests.

The following brief outlines of cases are placed on record to add to the growing list of reported disgerminomas. An analysis of such reports should prove useful in the final summation of the clinical and pathologic behavior of this group.

10 cm. in diameter were found. No other tissues were involved but there was some gland enlargement." The specimens were sent for study to the Department of Pathology, University of Georgia.

Pathologic Report.—Bilateral malignant tumors of the ovary; mesothelioma (reclassified dysgerminoma).

CASE 4.—A young white female, aged twenty-one, was admitted to the Oglethorpe Private Infirmary, Macon, Georgia, December, 1936, with nausea and vomiting of ten days' duration and abdominal swelling for the past three weeks. She was married one year ago, has never been pregnant and gave a history of normal menses except for the last period which was eight days late. Physical examination revealed essentially female development with normal genitalia and no evidence of masculine stigmata.

Operative Note.—Laparotomy revealed a growth the size of a small grapefruit arising from left ovary, with extensive invasion and spread into the retroperitoneal

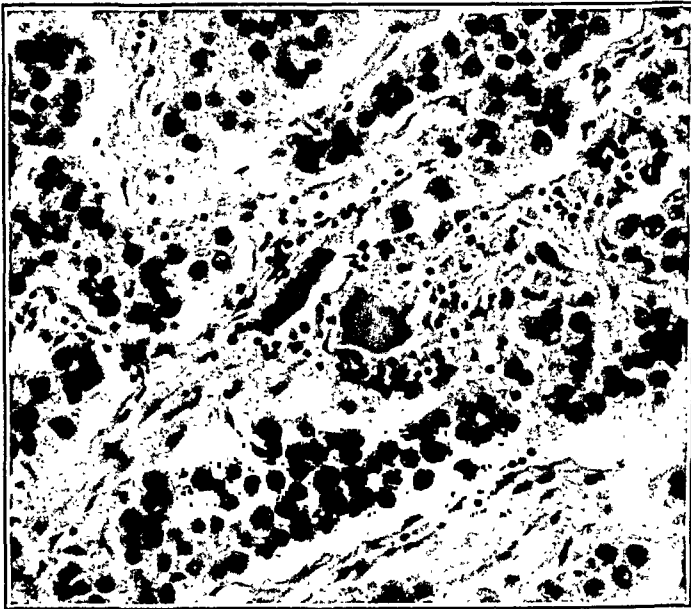


Fig. 6.—Case 5. Showing the pseudotubercle with the giant cell. This is an occasional feature observed in dysgerminomas. Note the characteristic cellular arrangement and the lymphocytic infiltration of the connective tissue stroma.

tissues and involvement of the mesentery. The growth was soft and friable and infiltrated. As much of the primary and metastatic growths were removed as was possible. The specimens were sent to the Department of Pathology, University of Georgia, for histologic study.

Pathologic Report.—Dysgerminoma (malignant). A course of radiation therapy was suggested.

CASE 5.—A young white female, aged twenty-one, married two months, was admitted to the Washington General Hospital, Washington, Georgia. She first noted pain in her right lower quadrant six months ago. Lately there had been a gradual increase in size of the abdomen. Her menstrual periods had been regular until two months ago, since which time she had not menstruated. It was observed that the breasts were fairly well developed, but there was a masculine distribution of the pubic hair. At laparotomy two large ovarian masses, measuring 20 cm. and 15 cm. in diameter, respectively, were removed. The uterus appeared small and

Postoperative Course.—Radiation therapy was given to the pelvis. Patient left the hospital in fairly good condition. She was readmitted two months later with generalized carcinomatosis and died with clinical evidence of cerebral metastases.

CASE 2.—An unmarried white female, aged thirty-five, was admitted in June, 1925, to the Edgecombe Hospital, Tarboro, N. C., with a history of a tumor palpable through the abdominal wall. A laparotomy was performed and a right ovarian tumor the size of a grapefruit was removed along with a small fibromyoma of the uterus. Specimens were sent to the Department of Pathology, University of Georgia, for examination.

Pathologic Report.—(a) Solid carcinoma of the ovary (reclassified dysgerminoma). (b) Fibromyoma of the uterus.

The patient recovered from the operation and was soon married. Six months later, however, she was again hospitalized and a second laparotomy revealed a



Fig. 5.—Case 4. Showing the sectioned appearance of an area of the dysgerminoma undergoing necrosis with cavitation and hemorrhage.

malignant growth of left ovary adherent to adjacent structures and extending into the ileum. Removal of the ovary and resection of the small intestine were performed and the specimens again sent to us for study.

Pathologic Report.—(a) Solid carcinoma of the ovary (reclassified dysgerminoma). (b) Secondary metastases to intestine.

CASE 3.—A young negress, aged twelve, was admitted to the Aiken Hospital, Aiken, S. C., Oct. 21, 1931, with acute abdominal distention, fever, nausea and vomiting. A history was obtained that three months had elapsed since her first and only menstrual period. Ten days prior to admission she was first seen by her physician who made the following note. "She was in a semi-conscious condition. The abdomen was distended and rigid. The pelvic examination was unsatisfactory but masses in both adnexa could be palpated. The white blood cell count was 20,000. Pulse was rapid and temperature was 100° F. She was apparently very toxic." She died one day following admission and permission for an autopsy limited to the pelvis was obtained. "Bilateral solid ovarian tumors each measuring

and invasion. These neoplasms are as frequently bilateral as unilateral. The sectioned surface presents a smooth, solid, homogeneous pale brain-like appearance. The tissue is very soft and friable. Hemorrhagic and yellowish discolored areas of degeneration and necrosis are frequently present.

B. Histologic study reveals a uniform picture of large cells with vesicular hyperchromatic round nuclei. The cytoplasm is scanty and is faintly stained. Mitotic figures are frequently seen. The cells are arranged discretely in small alveoli, in narrow cords of cells or lie loosely apart in a very fine and scant stroma. Trabeculas of loose edematous, poorly vascularized connective tissue are to be seen. These are often diffusely infiltrated with small lymphocytes. This lymphocytic infiltration is characteristic but is not always noted. Occasional giant cells and large macrophages filled with cellular débris, lipid globules, fragmented nuclear material are found. For detail study frozen sections are preferable since the tissue shrinks considerably with paraffin embedding. Sudan stains reveal occasional lipid filled cells.

C. Clinically these tumors grow rapidly and may reach a large size within a period of two to three months distending the abdomen. When degeneration occurs, fever, nausea, and vomiting with abdominal pain may become prominent symptoms. Changes in the menstrual cycle such as oligomenorrhea and dysmenorrhea, or amenorrhea may be present. Marked breast hypoplasia, infantile uterus and undeveloped external genitalia are commonly seen. Asthenic, sexually neuter females as well as hermaphrodites often harbor this tumor.

SUMMARY

Many ovarian neoplasms formerly designated alveolar large cell carcinoma, round cell sarcoma, seminoma ovarii, embryonal carcinoma, etc., fall into one classification, i.e., the disgerminomas. These neoplasms are peculiar to young women, the ages of the five patients herein recorded are twelve, twenty-one, twenty-one, thirty-four, and thirty-five. The disgerminoma arises from cell rests misplaced at the time of asexual embryonal growth of the gonad when the mesenchyme is undifferentiated and neutral. Hence this tumor may have its counterpart in the testis as well as in the hermaphroditic gonad. The disgerminomas do not exert any hormonal influence, however stigmas of hypoplasia and infantilism are frequently observed in patients harboring such neoplasms.

The surgical pathology of this neoplasm is distinctive. They occur bilaterally as frequently as unilaterally and appear as solid encapsulated or circumscribed lobulated tumors which have a peculiar doughy consistency. Sectioned surfaces are smooth, soft, friable, and have the characteristic appearance of brainlike substance. Microscopically round cells with large deeply staining nuclei and clear cytoplasm lie discretely

infantile. Extension of the growth into the retroperitoneal structures was noted. Several pieces of this neoplastic tissue were excised at operation. This material was sent to the Department of Pathology, University of Georgia, for study.

Pathologic Report.—Bilateral disgerminoma with invasion and extension.

ANALYSIS OF CASES

The age incidence in this series is characteristic. It is a tumor of the young woman as is indicated by the ages, twelve, twenty-one, twenty-one, thirty-four, thirty-five. In three of our patients it was unilateral, in one, however, the other ovary was later involved. In two the newgrowth was bilateral. The rapidity of growth of the tumors can be judged from the relatively short duration of symptoms. The menstrual cycle appeared to be disturbed once the tumor had developed to any size.

In Case 1, the mother of two children and married seventeen years, there was a sudden change from a normal and regular menstrual cycle to a very scanty and painful one for a period of one year before operation. In this patient the uterus (Fig. 1) was markedly hyperinvolted as to suggest a reversion to infantilism. Various authors have stressed the point that the disgerminoma in some manner retards development and is responsible for female hypoplasia. Of the five cases reported by Meigs,⁵ one case was that of a female aged twenty-five who had never menstruated and had marked genital and breast infantilism. In Frankl's⁶ two cases, one patient had a normal uterus, the other a rudimentary one. A large proportion of disgerminomas, however, fully 35 of 64 tabulated by Fauvet, have occurred in individuals with presumably normal sex development.

One salient feature of our small series is that none of the neoplasms were benign. One died with generalized metastases in spite of radiation therapy, another had metastases to the other ovary and small intestine, a third was bilateral with presumable regional lymph node metastases, and a fourth and fifth had extensive retroperitoneal invasion. This tumor is apparently frequently malignant even when unilateral. This point is at variance with other investigators (Meigs and Schiller). Schiller emphatically states that most of the unilateral disgerminomas are benign and exhorts us not to perform total extirpation in young women who hope for subsequent childbirth, nor to add radiation therapy with resulting castration of the patient. He advises radical measures only when a definitely positive diagnosis of malignancy can be made, not microscopically, but clinically by secondary deposits on the serosal surface of the uterus, peritoneum or the presence of ascites.

Béclère⁷ states that this neoplasm is characterized by its extreme radiosensitivity and advises the administration of deeply penetrating well-filtered x-rays projected at a distance and given in fractional doses over a prolonged period. In Meigs' series one patient who had peritoneal metastases died one and one-half months following radiation therapy. He nevertheless concludes: "this tumor which looks very malignant is apparently not severely so, as of five cases that have come to our attention, four are alive and well over four years."

SURGICAL PATHOLOGY OF DISGERMINOMA

A. Grossly the disgerminoma appears as encapsulated or circumscribed lobulated tumors of variable size with a characteristic doughy consistency. They may be freely movable in the pelvis or may be densely adherent to adjacent structures as a result of local extension

tates multiple operative procedures. It is emphasized by Frank and Geist that the construction of an artificial vagina is justified only in patients either married, planning to be married, or in single individuals with strong sex impulse.

The present case occurred in an attractive patient of definite feminine appearance, distribution of hair, with fairly typical external genitalia and complete absence of vagina. Upon rectal examination no pelvic structures were palpated which suggested the existence of a uterus or of gonads. This patient had normal feminine psychologic outlook and libido. She had apparently normal excitability centered in the clitoris and in the neighboring erogenous zones. There was a small dimple at the site of the normal vagina. This patient had a

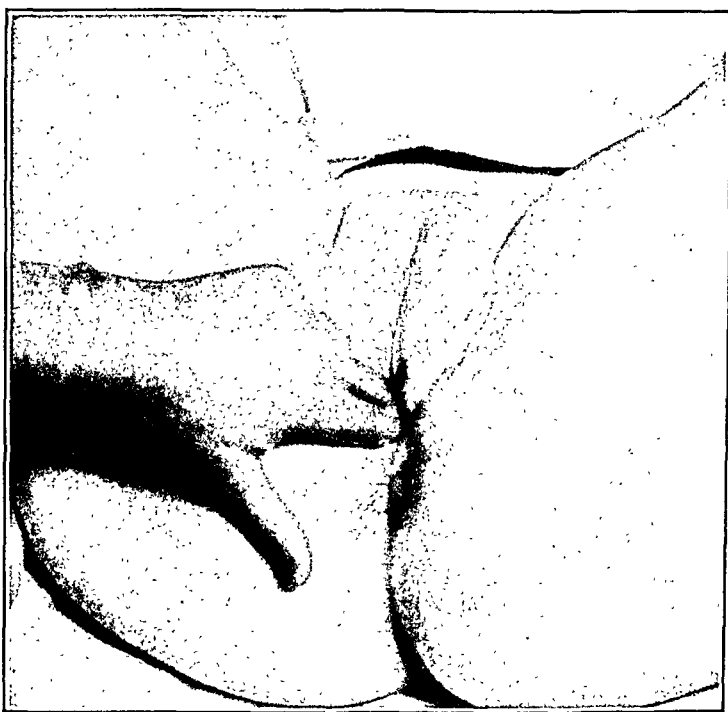


Fig. 1.—Appearance of vagina after failure of first operation by the Graves method, i.e., flap transplantation, employing labia minora and full thickness skin grafts from internal aspects of the thigh.

doubtful history of menstrual molimina and some indefinite bleeding from the rectum on two separate occasions. She was well nourished, having normal distribution of hair, and was normally feminine in contour and habitus. The clitoris was normal in appearance, labia minora small, and the urethral orifice large.

OPERATION

Operation was attempted by the Graves technique, four flaps being made from the labia minora, their twofold thickness being split, and two racket-shaped flaps from the inner aspect of the thigh, used for the upper and lower transplants, respectively. Transverse incision was made in the perineum, approximately $1\frac{1}{2}$ inches above the rectum. Rectal examination revealed nothing palpable suggesting ovary

apart in a scanty avascular stroma. Connective tissue trabeculas diffusely infiltrated with lymphocytes irregularly lobulate the neoplasm. However, this lymphoid feature may be lacking.

The unilateral tumors are said to be benign, nevertheless the three unilateral cases in this series proved to be malignant.

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THE CONSTRUCTION OF AN ARTIFICIAL VAGINA BY THE TUBE GRAFT METHOD*

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THE problem of the formation of an artificial vagina has been attacked in the past most often by the relatively dangerous methods of intestinal resection, employing either the small bowel (Baldwin-Gersuny) or the operation of Popow-Schubert using the resected portion of the lower rectum as the vagina. These operations naturally carry a relatively high mortality rate and in spite of the fact that they are best adapted to the treatment of this anatomic anomaly, the tendency more recently has been for gynecologists to attempt some form of plastic transplantation of skin flaps (Graves, Davis, Cron, Grad, Frank, and others).

The use of pedunculated skin flaps with immediate transplantation was employed successfully by us in one case reported in 1934. This patient has since married and has satisfactory coitus. Complete epithelization of the reconstructed vaginal vault, however, was difficult to achieve and the final length of the vagina after the period of complete healing had taken place was slightly less than three inches due to contraction.

In a second case performed by the same technique the lower flaps from the inner aspects of the thighs did not take and were lost almost completely in the resultant slough.

With this in mind it seemed advisable to attempt the procedure reported by Frank and Geist in 1927 with the report of additional cases in 1932. The principal objection to this procedure is that it necessi-

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and was left attached at both ends. The cut edges were sutured allowing the skin surface to remain outside, employing interrupted silk sutures. The defect on the thigh was approximated with stay sutures of silkworm gut, and the skin edges were closed with interrupted silk sutures. This defect healed satisfactorily (Fig. 2).

Two weeks later under gas anesthesia the distal attachment of the flap was detached further, approximately 50 per cent of the distal attachment being severed. The patient was discharged on May 29, 1935. Approximately six weeks later the patient was readmitted and the flap almost completely severed from its distal attachment. The skin was carefully prepared, and its bacterial flora reduced so far as possible by moist packs of phenylmercuric nitrate solution.

THIRD OPERATION

Examination of the outlet revealed the scars of previous plastic repair. The vaginal orifice was extremely small, admitting the index finger only up to the knuckle. The urethral orifice was approximately normal. A transverse incision was made in the perineum and with a sound in the bladder, the index finger of the left hand in the rectum, the rectovaginal septum was dissected. This was performed with some difficulty as the rectum and bladder were in extremely close approximation. There was very little bleeding. Dissection was carried out rapidly, only one large blood vessel being encountered on the left side of the vesicorectal septum. The "satchel handle" flap on the inner aspect of the left thigh was excised from its distal attachment and was cut along the original line of suture. This was inverted, turning "the skin side inside," the fat trimmed off, and it was sutured with interrupted fine catgut sutures about a rectal speculum, three inches in length, equipped with a phalange at its external end. Two sutures of No. 2 chromic catgut were brought through the length of the speculum through the apex of the sutured flap and one long suture beneath to aid drainage. The edges of the vaginal flap were approximated to the skin margins as uniformly as possible. The rectal speculum was held in place by guide strings of cable silk. A Pezzer catheter was placed in the bladder.

Eight days later when the speculum was removed, the grafts had taken and there was some slight sloughing immediately at the margin of the skin edge in the vagina. The retention catheter was removed on the tenth day. Saline douches were commenced on the tenth day. Discharge was rather marked. The patient was allowed out of bed on the fifteenth day, and external appearance of the vagina was quite good. The vagina admitted the index finger full length. Examination revealed the entire graft had taken, but there was a granulating area, at the apex of the new vagina. The patient was discharged and instructed to come in every two weeks for examination and manual dilatation.

The patient was examined and the vagina digitally dilated approximately every two weeks during the succeeding year. The scars of the previous plastic operation showed marked softening and the skin was in very good condition. Approximately six months after operation it was necessary to make a small incision in an annular contraction about the orifice most marked where the tubular flap had entered the vagina. The incision was made approximately an inch in the vagina into the scar tissue. Bleeding was slight.

This patient was followed carefully and was examined bimonthly during the succeeding seven months. There was a tendency toward contraction of the granulating area and foreshortening of the vagina at the end. This, however, did not become serious. At her final examination, July 1, 1936, the vagina was approximately three inches in length, soft, pliable, free from tenderness. It was fully epithelized, free from hair and marked scarring (Figs. 3 and 4).

or uterus. With a sound in the bladder and the index finger of the left hand in the rectum, careful dissection was made between the rectum and bladder admitting two fingers to a point as far distal as could be reached with the middle finger, carefully avoiding injury to the rectum or bladder. Several fairly large vessels were encountered, which necessitated suture.

The previously described flaps were sutured in place according to the method described by Graves and Pemberton.

The postoperative course was uneventful but the grafts did not take well. The lower pair were almost completely lost by slough.

The patient was readmitted to the hospital Jan. 27, 1935 approximately three months later. At this time in spite of numerous attempts at dilatations, the vagina was found to be markedly contracted, admitting only one finger to a point $1\frac{1}{2}$ inches from the introitus where there was a stricture. This dilated fairly readily and the vagina was found to be three inches in length with a diameter of only about 2 cm.



FIG. 2.—Tubular graft (satchel handle) showing distal attachment almost separated.

This patient was examined again two months later when it was found that due to scar tissue contraction, the operation had practically been a complete failure (Fig. 1).

On May 7 the patient was readmitted to the hospital, and it was decided to attempt the Frank and Geist method. This was reported in 1927 and 1932 with five cases wherein by successive steps a tubular flap is made which is then undermined, eventually inverted and implanted as a pedicle graft. The disadvantage of the method is the long period of hospitalization and the dilatation which must be scrupulously followed afterwards but the operation offers a better chance of success.

SECOND OPERATION.

On May 7, 1935 examination revealed a small opening at the vaginal site merely admitting one finger to the knuckle with marked scar tissue. On the left medial aspect of the thigh a full-thickness skin flap was undermined, beginning at a point approximately one inch from the labia minora, seven inches long, three inches wide

This patient has since married and normal coitus mutually satisfactory has been possible. The vagina is completely epithelized. The patient has experienced normal orgasm.

This method apparently stands a better chance of being successful than any method of immediate transplantation at a single stage and offers a better probability of resulting in a relatively deep pliable vagina which may be functionally adequate.

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RESULTS OF SKIN TESTS FOR PREGNANCY

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IN 1930 Porges and Pollatschek¹ suggested the utilization of the chorionic (anterior pituitary-like) hormone as a skin test for pregnancy. They reasoned that an intradermal injection of a small amount of this hormone should not give a skin reaction if a like hormone were present in the body. Hence, there would be no skin reaction in the presence of pregnancy because of the abundance of chorionic hormone in the system at that time. A negative skin reaction, therefore, would signify a positive test for pregnancy. They obtained correct reactions in 71.5 per cent of 90 pregnancies and 95.4 per cent of 150 nonpregnant patients.

Gruskin,² using his own hormonal preparation, reported correct reactions in 100 per cent of 158 pregnant, and 90 per cent of 39 nonpregnant, patients. Gilfillen and Gregg,³ using antuitrin-S, reported a series of 154 obstetric and gynecologic patients in whom the test was correct in every instance. Schwartz,⁴ who used antigen supplied by Gruskin, reported a group of 221 patients in whom the test was correct in 96 per cent of 155 pregnant women and 90 per cent of 66 nonpregnant women. He used 16 males as controls, in whom he obtained 100 per cent correct reactions. Schwartz stressed the importance of the pseudopodia rather than the presence of an erythema in positive reactions.

We have employed the intradermal test for pregnancy in 211 patients, 157 of whom were known to be pregnant. The technique followed by us was essentially that described by Gilfillen and Gregg.³



Fig. 3.—Pelvic examination, nine months after marriage, showing vagina approximately about three inches in length, admitting two fingers, in an ordinary pelvic examination.



Fig. 4.—External appearance of vagina nine months after marriage.

in 26 and negative for pregnancy in 22 of these patients, which constitutes a markedly lower percentage of correct reactions than we obtained when antuitrin-S was used alone. It therefore is possible that the reaction to antuitrin-S was influenced by theelin.

The results of the various investigators are given in Table II.

TABLE II

	PREGNANT		NONPREGNANT	
	PER CENT CORRECT	PER CENT INCORRECT	PER CENT CORRECT	PER CENT INCORRECT
Porges and Pollatschek	71.5	28.5	95.4	4.6
Gruskin	100.0	----	97.0	3.0
Gilfillen and Gregg	100.0	----	100.0	----
Schwartz	96.0	4.0	90.0	10.0
Hoffmann and Fouch	71.0	29.0	80.0	20.0

Our results tally more closely with those of the original investigators than with those of the American observers. We have no explanation to offer, but since we adhered strictly to details of the technique described and have been critical in the interpretation of skin reactions obtained we feel that our results are correct. Judging from our own experience, we feel that the intradermal injection of antuitrin-S as a test for pregnancy is not yet of such reliability that it can be recommended for replacement of the accepted biologic tests.

SUMMARY

1. Antuitrin-S given intradermally to 211 patients gave 71 per cent correct reactions in 157 known pregnancies and 80 per cent correct reactions in 54 nonpregnant patients.

2. Anterior pituitary liquid (Collip) gave 100 per cent incorrect skin reactions in 80 pregnant patients.

3. Antuitrin-S and theelin given simultaneously to 48 pregnant patients resulted in 54 per cent correct and 46 per cent incorrect reactions.

We wish to express our appreciation to Dr. Ludwig A. Emge for his assistance in the preparation of this paper.

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Weinzierl was at first skeptical of Knaus' contentions but he is now a firm believer of the Knaus theory of the safe period. He has observed a large number of couples who have successfully conducted their sex life according to the Knaus theory.

J. P. GREENHILL.

TECHNIQUE

Two minims of antuitrin-S are slowly injected with a tuberculin syringe into the skin of the flexor surface of the forearm. The resulting wheal should be round and have the appearance of pigskin. The reaction is read at fifteen-minute intervals. An area of erythema varying in size up to 35 or 40 mm. with the formation of pseudopodia indicates that no chorionic hormone is present in the patient and the reaction therefore is negative for pregnancy. If, on the other hand, no local reaction occurs, it indicates the neutralizing effect of chorionic hormone and therefore the test is positive for pregnancy.

Table I shows our results.

TABLE I

CLINICAL DIAGNOSIS	NEGATIVE FOR PREGNANCY	POSITIVE FOR PREGNANCY	TOTAL
Pregnancy	45	112	157
Pelvic inflammatory disease	14	0	14
Pyelitis	4	0	4
Normal female	4	0	4
Normal male	5	2	7
Fibromyoma	3	2	5
Carcinoma of cervix	1	2	3
Abortion, spontaneous	1	2	3
Abortion, incomplete	2	1	3
Nephritis and pregnancy	1	0	1
Chronic cervicitis	1	0	1
Ectopic pregnancy	2	2	4
Hyperplasia of endometrium	2	0	2
Postpartum, day V	2	1	3
Totals	87	124	211

Occasional latent skin reactions were observed. They are not of importance as far as the immediate reading of the test is concerned, and probably are not significant. We noted this latent reaction in 18 of the pregnant patients, one of whom developed a marked induration and erythema as late as twenty-four hours after the injection.

Since the commercial preparation of Antuitrin-S supposedly contains the same hormone as anterior pituitary liquid (Collip),* we were interested to learn if the latter could be used for this test. We therefore tested 80 known pregnancy patients with intradermal injections of 0.1 c.c. The resulting reactions were 100 per cent incorrect, and considerable soreness was produced locally. Presumably, anterior pituitary luteum does not contain any estrin, but since we obtained such a marked skin reaction we wondered whether it might be due to the presence of a small fraction of this ovarian hormone. Therefore, we selected 48 patients known to be pregnant and gave each an intradermal injection of 0.1 c.c. aqueous theelin and a similar amount of Antuitrin-S at different localities in the arm. Theelin gave as marked a dermal reaction as anterior pituitary luteum, but the local erythema and induration disappeared more rapidly, so that a skin reaction was present at the end of one hour in only 14 patients. The reaction was positive for pregnancy

*Anterior pituitary liquid kindly supplied by Messrs. Ayerst, McKenna and Harrison.

remarkable of all, in most cases it develops more or less pointed bulges opposite each other at the widest part and farthest from the cervical tear (see Fig. 1, *a, b, c, d*). Without a doubt these correspond to the areas over which the tubes arise. This assumption is furthered by the fact that several unopened pregnant uteri, hardened in formalin, when bisected revealed the identical bulges over these areas (Fig. 2).

The average full-term sac is found to hold between three and five liters of fluid; a twin pregnancy sac held almost seven liters, and several cases of polyhydramnios, an equal amount.

From a study of the distended sacs directly and from clay models of a hundred of them, it is seen that the most common placenta is more or less circular and lies between the uterine cornua and on the relatively flat anterior or posterior wall. It seldom extends over the dividing line



Fig. 2.—Photograph of placental half of five months' pregnant uterus containing fetus and unruptured amniotic sac and hardened in formalin before bisecting along lateral surface. Placenta here lies between the bulging cornual areas.

between anterior and posterior walls either at the side or over the apex of the fundus and when it does, it is most likely to be bipartita or succenturiata or placenta spuria.

This method is ideal for the study of abortion sacs and often reveals the cause of the termination of pregnancy otherwise unsuspected. It shows a definite tendency for early placentas to be relatively larger in area than at full term, and from few cases so far studied a tendency to atypical location of implantation in the uterus, i.e., cornual or cervical rather than in the anterior or posterior wall which are relatively flat and probably contain the best decidua for implantation and subsequent nourishment of the ovum.

This method is of value in the study of placenta previa and reveals it to be more common than clinically diagnosed. However a check of the history of labor usually reveals vaginal bleeding prior to delivery.

DESCRIPTION OF A NEW METHOD OF STUDYING PLACENTATION BY AMNIOTIC SAC DISTENTION

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IF CARE is exercised in delivering the placenta it is possible to obtain the placenta and fetal membranes quite intact so that the sac is complete with the exception of the opening over the cervical area through which the fetus emerged at birth.



Fig. 1.—Four photographs of the same full-term sac in a glass jar of water showing (a) placenta located on one anterior or posterior wall between the two cornual bulges, (b) reverse face, (c) lateral view of the surface with the more prominent bulge, (d) opposite lateral view.

Now by the simple procedure of submerging this sac in a tank of water up to the cervical rupture and then introducing into the cavity of the sac a known quantity of water to fill and distend it to its capacity, it is found that the sac assumes the exact shape of the distended uterus from which it came. The sac takes on a rough pyriform shape and most

OBSERVATIONS ON THE EFFECTS OF URETHANE AND BARBITURATES ON SMOOTH MUSCLE

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TO RELIEVE the pain of childbearing without delaying the progress of labor is one of the commonest problems of the anesthetist and a constant one for the obstetrician. The barbiturates have come into rather general use as sedatives, analgesics and pre-anesthetics. Repeated clinical observations have indicated that Dial (di-allyl-barbituric acid) not only seemed not to slow down labor, but actually seemed to hasten the process.¹⁻⁴ Dial, as commercially available, comes in an ampule containing 4 times as much urethane (ethyl carbamide) as di-allyl-barbituric acid. The urethane is included for the sake of increasing the solubility. It seemed possible that the urethane might have altered or contributed to the action of the mixture. External hysterographic studies were undertaken, are still in progress, and will be reported later.*

In the meantime a certain amount of purely laboratory investigation of the action of urethane on smooth muscle has been done. For a comparative working basis such experiments are indicated, with all respect for the recognized differences between isolated smooth muscle tissue in an artificial bath and the human parturient uterus. In clinical labor the state of the central nervous system, the ability to cooperate, the help of voluntary abdominal muscles, and, especially, the highly active physiologic state of the uterine muscle itself are all powerful factors. Nevertheless, the direct action of drugs concerned on smooth muscle must be the starting point for comparative study.

There is a general impression among physiologists and other laboratory workers that urethane, in animal experiments, interferes less with normal reflex responses than do any of the other common anesthetics.

Previous reports⁵ have indicated that isolated intestinal segments were relaxed only by concentrations as high as 1:200 to 1:100. Repeated checking in this laboratory has found the concentration of urethane necessary for depression of uterine or intestinal muscle to be about 1:150. Since the usually employed clinical dose of dial represents roughly a urethane concentration of 1:5,000, muscle depression by the urethane component would not be expected. Di-allyl-barbituric acid alone has about the same smooth muscle depressing power as has amytal (iso-amyl-ethyl-barbituric acid); i.e., 1:40,000 or greater concentration is necessary

*Suggestion of the problem and guidance of the work, of which this report is a part, was given by Professor Graffagnino of the Department of Gynecology of this institution.

Not enough cases of placenta circumvallata have been found to make any definite statements in regard to their location but, from the cases recorded, this method in the future should be of greatest value in elucidating this remarkable condition.

If the obstetrician will mark with a dye the anterior portion of the sac as it emerges from the vagina, he will be able to further localize the placenta in the uterus as to anterior and posterior wall.



Fig. 3.—Photograph of three months' abortion sac showing the cervical and two cornual defects in the decidual covering of the distended sac.

The pressure of the fluid in the sac may be varied from 1 cm. to 20 cm. of water without causing noticeable volumetric changes in the sac. Consequently fairly accurate studies may be made in regard to the relation of area of placenta to area of uterine cavity.

A perusal of the literature reveals no mention of such a method of study.

Oyrzun, Romeo Cadiz: A Case of True Hermaphroditism (Ovary-Testes) in the Human, *Bol. Soc. Chilena de obst. y ginec* (Buenos Aires) 1: 117, 1936.

A case of true hermaphroditism with ovotestes is presented. The patient dying of pulmonary tuberculosis was studied postmortem and autopsy material established the diagnosis. The patient had a typical masculine voice, and well-developed breasts. The genitals revealed feminine distribution of hair, a hypospadiac penis and a small vagina. The patient had an attraction for the female sex but had been intersexual.

CHEMICAL TEST FOR THE DETERMINATION OF RUPTURED MEMBRANES

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RECENTLY there has been considerable interest in the establishment of accurate tests for the determination or confirmation of rupture of the amniotic sac. Several investigators have succeeded in evolving tests which are apparently sufficiently accurate to be of value.

The tests have been based on the fundamental facts that normally the hydrogen ion concentration (pH) of the vaginal secretion ranges around 4.5 to 5.5 and the pH of the amniotic fluid is usually 7.0 to 7.5.

On the assumption that the pH of the vaginal secretion will change when it is contaminated with the escaping amniotic fluid following rupture of the membranes, the determination of the hydrogen ion concentration of the vaginal secretion would seem, therefore, to be an index to the status of the amniotic sac relevant to continuity.

Recently, there has been marketed an indicator test paper* impregnated with sodium dinitro phenylozonaphthol disulphonate, commercially known as nitrazine paper. With these papers is furnished a color chart comprising a pH range from 4.5 to 7.5. The papers are set at pH of 6.0. These indicator papers were intended for use primarily to determine the reaction of urine.

In view of the fact that the nitrazine papers with the accompanying color chart comprise a pH range sufficient to cover both the pH of the vaginal secretion and that of the amniotic fluid, it seemed appropriate to use this method for the determination of the status of the amniotic sac. Consequently, this method was tried on a small number of patients admitted to the Baltimore City Hospital with a history of premature rupture of the membranes. Those cases which revealed the reaction of the vaginal secretion to be at a pH of 6.0 or above were found, by their subsequent course, to have given a correct history of ruptured membranes. Those cases in which the pH of the vaginal secretion was below 6.0 were found, by the same criteria, to have submitted a false history of ruptured membranes. The test seemed to have possibilities and it was planned to run a series of consecutive cases to control and confirm the accuracy of the method.

TECHNIQUE

Fifty patients, consecutively admitted to the delivery suite of the Baltimore City Hospital, were used in this series. The pH of the vaginal secretion was determined by inserting a sterile cotton-tipped applicator deeply into the vagina, and after withdrawal, the cotton tip was touched to a strip of the nitrazine paper and the paper then compared with the color chart. If, during the course of labor in the first stage room, the membranes ruptured spontaneously, the test was repeated. If the membranes ruptured when the patient was draped on the delivery table, the test was not repeated.

*Made by E. R. Squibb and Sons Company, New York.

for relaxation.⁶ The usual dial dose is approximately equivalent to a concentration in the blood stream of 1:22,500, well within the depressing range. There must, however, be some reason for the "clinical impression" that delivery is hastened by its use.

Attempting analysis, about 30 experiments have been done on isolated rabbit intestine and guinea pig uterus, using sodium amytal alone and sodium amytal plus 400 per cent urethane in concentrations ranging from minimal effective to virtually paralytic.

In no instance was there any indication that the added urethane contributed in any way, in either direction, to the effect of the amytal.

Comparison of some accepted approximate figures: if urethane depresses smooth muscle at a concentration of 1:150, and amytal depresses smooth muscle at 1:40,000, the ratio of smooth muscle depression is 1:266. With 4 times as much urethane as amytal in the mixture, there is attributable to the urethane component an extra 1.5 per cent muscle depression. Calculated roughly from effective dog doses, amytal is 30 times as anesthetic as urethane. With 4 times as much urethane as amytal, the urethane component adds an extra 13 per cent to the anesthetic power of the combination.

It should further be remembered that delivery may be accelerated clinically by relaxation of the cervix, despite a certain amount of possible potential smooth muscle depression.

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Hollosi, K.: Appendicitis and Menstruation, Monatsehr. f. Geburtsh. u. Gynäk. 106: 187, 1937.

The author found that in a series of 159 women operated upon for appendicitis, 68 per cent were operated upon during the premenstrual and postmenstrual periods, 17 per cent during actual menstruation and only 15 per cent at other times during the menstrual cycle. He believes that the hyperemia which occurs during the premenstrual period and actual menstruation can imitate the symptoms of appendicitis. He is of the opinion that the hyperemia of the appendix is due to the corpus luteum hormone. He observed cases in which dysmenorrhea disappeared after appendectomy.

J. P. GREENHILL.

part of the first stage of labor, when each of the patients was having a rather unusually large amount of bloody show. However, at this stage of labor the question of the status of the amniotic sac is not such an important one as a rule, and, moreover, at this stage the cervix is usually sufficiently dilated so that the question can be settled by the examining rectal finger.

With the technique as described above, it would seem that the possibility of a false reading because of contamination by urine is negligible. The deep insertion of the cotton-tipped applicator into the vagina should insure against this.

It is the policy in this clinic to shorten the interval between the premature rupture of the amniotic sac and delivery of the patient as much as possible. By this it is meant that a patient who presents herself with what we feel is an assured history of ruptured membranes is given a medical induction. This policy is based on the belief that the shortest interval between the membrane rupture and delivery serves the best interests of the patient. In those patients, who present themselves and "think" their membranes have ruptured without labor pains, and in whom it is found that the cervix is closed, it would seem that this test is of great value.

SUMMARY

1. The determination of the pH of the vaginal secretion may be used as a test for the determination of the rupture of the amniotic sac.

2. A simple technique has been evolved by using nitrazine test papers by which this determination may be accomplished satisfactorily.

3. A pH of 6.0 or above indicates ruptured membranes. A pH below 6.0 indicates unruptured membranes.

4. A false reading is likely to be encountered in a patient with intact membranes who has an unusually large amount of bloody show. In the early stages of labor, however, at a time at which the test is of most value, it is accurate.

5. The test lends itself ideally in those patients who present themselves with a history of possible rupture of the membranes, not in labor, in whom the usual clinical examination is not adequate to confirm the history.

CARCINOMA IN AN ADENOMYOMA OF THE UTERUS

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ACCORDING to Ewing,¹ leiomyomata of the uterus are the most common of all tumors; adenomyomata of the uterus are relatively rare. Malignant changes in these tumors seldom occur. Indeed, up to 1929, only 26 such cases have been reported,² and none since. Of these, 19 showed carcinomatous, 5 sarcomatous, and 2 both types of changes. Metastases to distant organs occurred in 5 instances. The following is a report of an adenomyoma with carcinomatous change in a uterus which was removed at operation. The patient subsequently made an uneventful recovery.

Clinical History.—M. J., a forty-year-old white woman, was admitted to The Jewish Hospital of Brooklyn on the service of Dr. E. V. Littauer, on Jan. 14, 1937, complaining of severe pelvic pain radiating to the thigh, associated with excessive bleeding at the menstrual periods for the past two months. She stated that for the past eight years she had dysmenorrhea; her periods were irregular and were associated with excessive bleeding and with occasional back pains radiating to the thigh. There was an occasional leucorrhea. She had had no menopausal symptoms.

RESULTS

In the series of 50 consecutive cases that were studied 11 of these patients were admitted with a history of ruptured membranes, and 39 gave a negative history on this point. Table I shows the results obtained with the test in the 39 cases of unruptured membranes. In 26 of these cases the pH of the vaginal secretion was 4.5. In 9 others it was 5.0 and in the remaining 4 it was found to be 5.5. Fourteen of these 39 patients had a spontaneous rupture of the membranes after admission while still in the first stage, and the test was repeated. Following the rupture in 3 cases the vaginal secretion revealed a pH of 7.0, and in 11 it was 7.5. The remaining 25 of the 39 cases were not tested because the membranes were ruptured at delivery.

TABLE I

PATIENTS ADMITTED WITH HISTORY OF UNRUPTURED MEMBRANES IN EARLY FIRST STAGE LABOR. 39 CASES

	ON ADMISSION		AFTER MEMBRANES RUPTURED		RUPTURE ON DELIVERY
	pH	CASES	pH	CASES	TABLE
	4.5	26	7.0	3	NOT TESTED 25
	5.0	9	7.5	11	
	5.5	4			
Total		39		14	

In Table II, the data are recorded on the 11 patients who were admitted with a history of ruptured membranes. In this group some were in early labor and others were not in labor. A record was kept of the time elapsing between the rupture of the membrane and the time at which the test was done. It will be seen from the table that the shortest interval was fifteen minutes and the longest nineteen hours. One of these patients first tested after an interval of nineteen hours had a very protracted labor and was tested again when the interval had reached twenty-nine hours, and the pH at this time was 6.0. The patient was delivered shortly thereafter.

TABLE II

PATIENTS ADMITTED WITH HISTORY OF RUPTURED MEMBRANES (INCLUDING THOSE IN LABOR AND THOSE NOT IN LABOR). 11 CASES

TIME ELAPSED BETWEEN RUPTURE AND TEST	pH
15 minutes	7.0
45 minutes	7.5
1½ hours	7.0
1½ hours	7.5
2 hours	6.0
6 hours	7.5
6½ hours	7.0
8 hours	7.0
12 hours	7.0
19 hours	7.0
*19 hours	7.0

*This patient was tested again twenty-nine hours after membrane rupture (still undelivered) and the pH was found to be 6.0.

The one enlightening fact relevant to the possibility of a false reading was brought out in 3 of the patients who went through labor with the membranes intact until delivery. These 3 cases showed the expected acid reaction on admission, but the reaction changed to an alkaline one (6.5, 7.0, and 7.5, respectively) in the latter

myometrium measured 1.5 cm. in thickness and was pale brown. In the opposite wall there was a nodule which was circumscribed by a narrow rim of pale brown myometrium. It was uniform and was composed of pearly gray-white interlacing bundles. In it were pinpoint depressions with pouting borders from which exuded some mucoid material. Both Fallopian tubes measured 8 by 0.5 cm. The fimbriated extremities were patent. The cut surfaces were not unusual. The right ovary



Fig. 3.—Photomicrograph of the wall of the uterus showing some overgrowth of the endometrium but no tumor involvement of the myometrium. (H. & E. X45.)



Fig. 4.—Photomicrograph of the tumor in the adenomyoma showing the general nature of the growth. (H. & E. X45.)

measured 5 by 4 by 1.5 cm., the left, 4 by 2.5 by 2 cm. Both contained numerous thin-walled cysts, up to 1 cm. in diameter.

A microscopic preparation through the wall of the uterus showed at one end a broad endometrium with many large tortuous glands in a loose tunica propria. The lining cells were columnar and varied somewhat in size and shape; in places they were heaped up into several rows. The lumina contained amorphous lavender staining material. There was no invasion of the myometrium. In the preparations through the tumor, there were zones composed of interlacing bundles of smooth

On admission, the physical examination was essentially negative, except for marked pallor of the lips and mucous membrane. The red blood cells were 3,100,000 per c.mm.; the hemoglobin was 45 per cent. The clinical impression was that she had a fibroma of the uterus and polyglandular dysfunction. On the day following admission, a transfusion of 750 c.c. of whole blood was given. At operation on January 18, the uterus was found enlarged to the size of a three months' gestation by

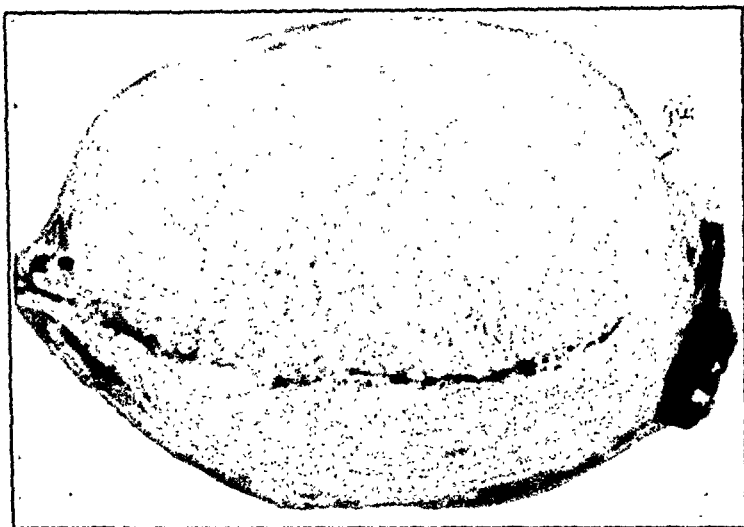


Fig. 1.—Photograph of the cut surface of the uterus showing the well circumscribed tumor.

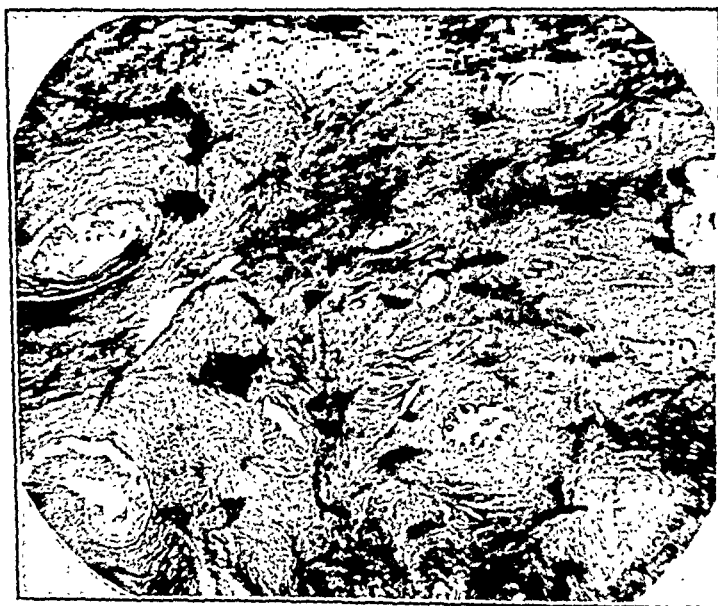


Fig. 2.—Photomicrograph of a portion of the adenomyoma uninvolved by carcinoma. (H. & E. $\times 15$.)

a fibroid. Both ovaries contained numerous small cysts; the tubes appeared normal. A supracervical hysterectomy and a bilateral salpingo-oophorectomy were performed by Dr. E. V. Littauer.

The specimen consisted of an ovoid-shaped uterus with attached tubes and ovaries. The uterus measured 14 by 11 by 9 cm. The external surface was smooth and glistening. The uterine cavity was 9 cm. long. The endometrium was pale and shaggy and not well demarcated from the myometrium. In the cut surface the

THE DIAGNOSIS OF TRICHOMONAS VAGINALIS*

A COMPARISON OF A CULTURAL METHOD WITH DIRECT EXAMINATION OF WET PREPARATIONS

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A NUMBER of authors have reported that protozoan parasites can be found more frequently if certain cultural methods are used than when direct examination is made of the material. Nevertheless, it has been noted previously³ that in the case of parasitic amebas, direct examination of the feces yields a larger number of positive findings than do cultural methods, and that all the problems of species identification pertain to amebas in cultures that attend the determination of species found on direct examination, and often some additional problems.

In a number of papers the culturing of material in which flagellates are suspected of being present has been advocated and claims are made that the cultural method reveals more positive findings than the direct method of examination.

With regard to *Trichomonas vaginalis*, Andrews¹ reported that "five of twenty positive cases did not show the presence of *Trichomonas vaginalis* either in the direct smears or the stained films, but in cultures a heavy growth occurred." She considered asparagine medium and agar-slope and serum-saline-citrate solution the best mediums. Karnaky² has advocated the cultural method for diagnosis of *Trichomonas vaginalis* and has reported having difficulty with distinguishing these parasites from pus cells when direct examination is made. He used "Hill's medium" which actually is Hogue's medium and stated that more positive results could be found by the cultural method than by direct examination.

In order to test the relative merits of these two methods, 250 consecutive examinations were made for the presence of *Trichomonas vaginalis*, using a cultural method and direct examination. Hogue's medium was first tried in a preliminary run of fifty cases, but the medium proved unsatisfactory both from the standpoint of manufacture and of revealing growth. The medium recommended by Powell⁴ was then used and it proved highly satisfactory.† The medium used must be considered satisfactory since luxuriant growths were obtained in nearly all instances and each time the parasite was found by smears, some degree of growth resulted except once.

*Submitted for publication, April 22, 1937.

†Loeffler's dried blood serum is weighed out in quantities weighing 0.06 gm., which are then put in ordinary 5 gr. (0.3 gm.) gelatin capsules. Modified Ringer's solution is then made up by dissolving 6.0 gm. of sodium chloride, 0.1 gm. of potassium chloride, 0.1 gm. of calcium chloride, and 0.1 gm. of sodium bicarbonate in 1000 c.c. of distilled water. Twice or thrice a week, as the medium was required in this study, 25 c.c. of this Ringer's solution was measured out and the contents of one of the gelatin capsules was added to it. When the Loeffler's serum was dissolved, 0.5 c.c. of fresh, Wassermann-negative human serum was added. Ordinary test tubes of 15 c.c. capacity, plugged with cotton, were used as culture tubes. About one loopful of rice starch was placed in the bottom of each tube and 6 to 8 c.c. of the liquid medium was then poured over it. It was not found necessary to sterilize this medium. No adjustment of pH was necessary, the pH, as determined colorimetrically with bromthymol blue, being approximately 6.8.

muscle cells in whorl-like arrangements; in some of these areas there were lumina empty or containing amorphous lavender staining material which were lined by columnar cells. In other zones imbedded in a dense fibromuscular stroma, were large irregular lumina with frequent infoldings and secondary papillary projections. The lining cells varied in size, shape, and chromatin content of their nuclei. Many were in a state of mitotic division. The lumina contained amorphous pink or lavender staining material. Preparations from the ovaries and tubes showed nothing unusual.

The pathologic diagnosis was "uterus, with cylindrical cell carcinoma, arising in an adenomyoma; Fallopian tubes and ovaries."

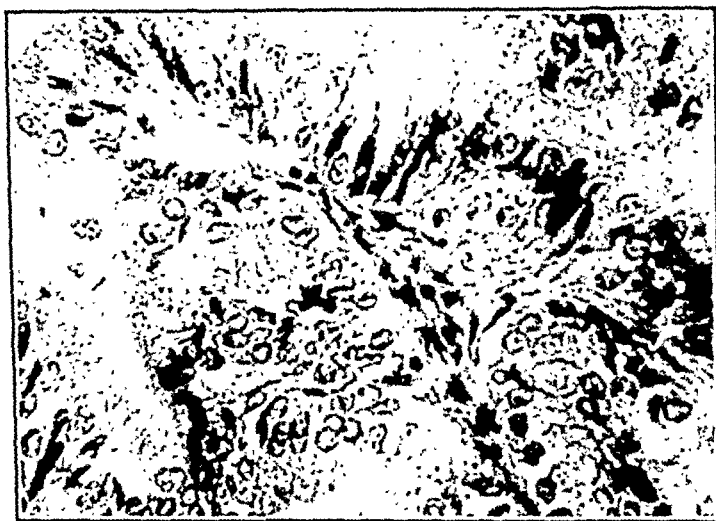


Fig. 5.—A higher magnification showing the type of cell making up the tumor. (H. & E. $\times 600$.)

Comment.—There are two possible interpretations in this case. It is either a carcinoma of the uterus with extension into a leiomyoma, or a carcinoma arising in an adenomyoma of the uterus. Of the two, the latter appears to be the more probable for the following reasons: In the first place, a carcinoma of the uterus which extended into a leiomyoma on one side should also have involved the opposite wall. Second, there are within the tumor nodule, zones composed of loose fibrous connective tissue resembling the tunica propria of the endometrium, in which well preserved lumina are seen containing some lavender staining, amorphous material, and lined by tall columnar cells.

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Carraro, Arturo: Spontaneous Rupture of an Imperforated Vagina, Clin. obstet. 13: 155, 1935.

The author reports a case of congenital imperforated vagina, unrecognized for thirty months following the initial menstrual period. He describes the resulting changes of the internal genitalia and the final spontaneous rupture of the vagina into the peritoneal cavity.

AUGUST F. DARO.

DERMOID CYST OF OVARY IN A CHILD FIVE YEARS OLD, WITH COMMENTS ON VALUE OF X-RAY IN THE DIAGNOSIS

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A REVIEW of the literature reveals that ovarian tumors are rare in children under ten years of age. They are still less frequent in children under five years old. Wiel¹ studied 60 cases in children of ten years up to 1904. Dermoid cysts were present in 21 cases, or 35 per cent. A further analysis of his investigation revealed 7 patients under five years of age; these cases had a mortality of 65.1 per cent. Downes² reviewed 26 cases of ovarian tumors from 1904 to 1921 in the same age group, of which 8 cases were dermoids. Further study revealed only 2 cases, five years or under. In Loeb and Levy's³ analysis of 35 cases from 1921 to 1931, there were 9 cases of teratoid tumors. Only 3 patients were under five years of age. Wakeley⁴ in 1933 reported 3 patients under 10 years of age, but none five years or under. He studied the records for twenty-five years of the Hospital for Sick Children, Kings College Hospital, and the Belgrave Hospital for Children, and found one case each in the latter hospitals, but no case in the first. Apparently, dermoids in children under five years of age are extremely rare. It is our purpose to report the occurrence of a dermoid cyst of the ovary in a child five years old, and to emphasize the value of the Roentgen ray in the diagnosis of a dermoid cyst of the ovary.

CASE REPORT

R. R., female, five years of age, was admitted to St. Peter's Hospital on Aug. 13, 1936. She had no family history of malignant disease. Both of her parents had always been in good health. She had scarlet fever at nine months, pneumonia with empyema at three years of age, pertussis two months prior to admission with no complications. The present illness at this admission revealed pain in the lower abdomen near the midline with no associated nausea or vomiting.

Physical examination showed a young white female poorly nourished, anemic, but not acutely ill. Teeth in rather poor condition. Tonsils enlarged and injected. Cervical glands on both sides were enlarged. Heart and lungs were grossly negative. Inspection of the lower abdomen presented a pyriform appearance with suppression of respiratory movements. The percussion note revealed tympany over the epigastrium and splenic flexure, likewise over hepatic flexure; dullness to flatness over both lower flanks with the suggestion of a fluid wave in lower abdomen. No venous enlargement was present in the abdominal wall. On palpation a tumor mass was felt which was semisolid, mobile, globular, nodular, insensitive, and did not seem to be adherent to the anterior wall. This tumor mass seemed to have its origin in the right side connected by a pedicle and freely mobile. It was 7 by 8 cm. in diameter. There were no nodular masses palpable throughout the remaining abdomen.

Roentgen ray of the abdomen revealed an oval-shaped tumor measuring about 8 cm. in diameter in the right side of the abdomen extending from the lower liver edge downward to below the iliac crest. There appeared to be plaques of calcification in this tumor mass. The calcified area is irregularly branched with areas of density somewhat suggestive of bone and rudimentary teeth development.

The preoperative diagnosis was right dermoid cyst.

The method of collecting the specimens in order to make the two methods comparable was to insert two sterile cotton swabs into the vagina and rotate them several times. One was then shaken off in a drop of physiologic salt solution on a slide, and a cover glass was applied. Search was made under a magnification of 100 diameters for from one to three minutes. Higher magnification was used for verification. The other swab was plunged into a tube of medium and the tube, with its swab, incubated for twenty-four hours, after which time wet preparations on slides were made and examined. The maximal growth was usually seen in twenty-four hours but occasionally not until forty-eight hours. The cultures were not held longer. Of the 250 females examined, 52 (20.8 per cent) proved to harbor *Trichomonas vaginalis* and of these cases, in 51 the parasite was found by the cultural method and in 51 by the direct smear method; one instance being missed by each method (Table I).

TABLE I. COMPARISON BETWEEN CULTURAL METHOD AND DIRECT EXAMINATION OF FRESH VAGINAL SECRETION FOR THE PRESENCE OF TRICHOMONAS VAGINALIS

SMEARS		CULTURES	
POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
51	199	51	199

It can be seen from the results that the cultural method possesses no advantage over a careful direct examination of vaginal secretion. Even if both methods are used on each specimen only an occasional additional positive finding will result, not enough to justify the additional time and expense involved in the cultural method. It is important that the examiner use low power magnification and that he be familiar with normal and pathologic vaginal secretions and, what is most important, that he be able to recognize the species *Trichomonas vaginalis*.

CONCLUSION

If fresh wet preparations of vaginal secretion are competently examined on slides, results will be satisfactory. By use of a cultural method the number of positive findings will not be sufficiently increased to justify adoption of such a procedure. Either method, in competent hands, should yield approximately the same results; the direct examination will be cheaper, less laborious and will yield results twenty-four hours sooner than the use of cultures.

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Pathologic Report.—The ovary showed a large cyst approximately 8 cm. in diameter, one section of this cystic mass showing dense tissue with calcification. This was proximal to fimbriated extremity and represented residual ovary. Mass was translucent and showed smaller cystic areas within the surface capsule. The cyst contained considerable amount of cholesterolin deposit and hair. Section of the wall showed dense connective tissue. In one section there was a structure closely simulating chorion stratified squamous epithelium and sweat glands.

The child made an uneventful recovery, and was discharged from the hospital on the fourteenth day. The child has been seen on several occasions since discharge and is in apparently the best of health.



Fig. 3.—Roentgenogram of tumor after removal. Opaque substance containing rudimentary mandible and teeth can be outlined.

In the above case, the preoperative diagnosis of a dermoid cyst was made and subsequently confirmed at operation by a roentgenogram of the abdomen, which clearly showed a rudimentary mandible with teeth (Fig. 2). A roentgenogram of the tumor was taken after extirpation which showed the same elements (Fig. 3).

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133 CLINTON STREET
38 LIVINGSTON STREET

The operation was under ether anesthesia. The abdomen was opened through a midline incision, about 4 inches long. A tumor about 7 by 8 cm. in diameter was delivered. The tumor was found to be a right-sided tumor of the ovary twisted on its pedicle. It was globular, semicystic and contained calcified material. On the



Fig. 1.—Illustrates the tumor opened with fluid contents removed. Cholesterol substance, hair, rudimentary maxilla, and teeth are shown.

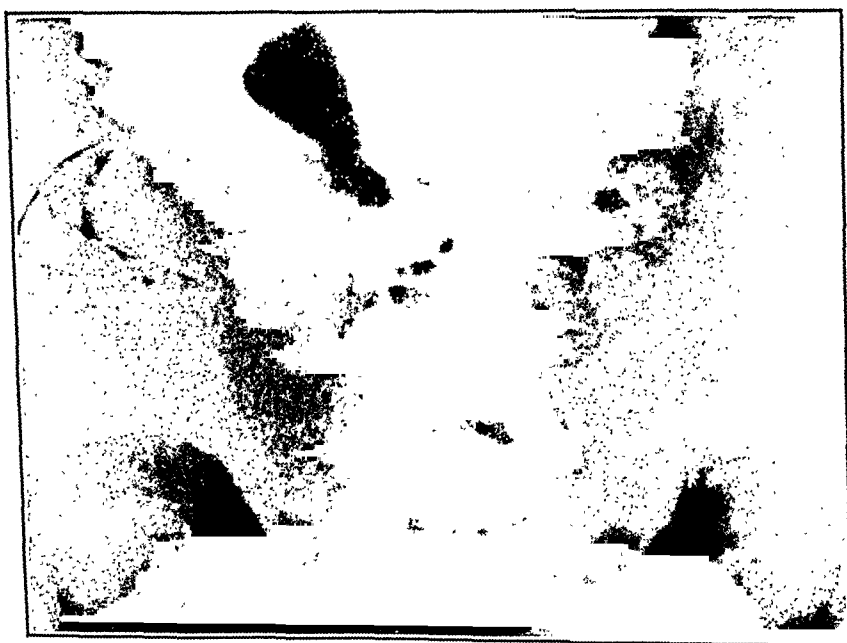


Fig. 2.—Roentgenogram of tumor before operation. Opaque substance containing rudimentary mandible and teeth can be outlined.

surface, there appeared some tissue resembling ovary. The pedicle was long and about 2.5 cm. wide, coming from the right broad ligament. The uterus was small and normal. The left tube and ovary were normal. The tumor was removed together with the right tube which was very much flattened out over the superior surface of the cyst (Fig. 1).

At 7:00 P.M. there had been little change. The patient was fairly comfortable. Temperature was 99.6° F. rectally. Abdominal and pelvic findings were still indefinite. The white blood count had dropped to 11,000, and we thought we could observe the patient some hours longer with safety.

By noon the next day, however, the patient had more pain. There was a temperature rise to 100° F. rectally, a rise in pulse rate to 104, and definite resistance of the right rectus muscle. We decided to explore the abdomen. Under ethylene and ether anesthesia, the abdomen was opened through a right rectus incision. Less difficulty was encountered from the obese abdominal wall than had been anticipated. A large, blue purple mass filling the right half of the pelvis (Fig. 1) presented itself immediately. It was easily delivered into the wound and was found to be a hydrosalpinx, the pedicle of which was twisted clockwise 3 full revolutions. There was considerable extravasation of blood into the right broad ligament and the ovary. The tube, ovary, and most of the broad ligament were removed and the stump of the broad ligament was peritonized. The appendix, which had been loosely adherent to the mass as well as to the cecum, was removed. Closure was in layers using chromic catgut and silk, and was not difficult.

Carbon dioxide was administered every hour postoperatively until hyperpnea appeared. Convalescence was uneventful except for some cough and temperature rise to 102° F. rectally, the second day. On the fifth day the patient was allowed to sit on the side of the bed. On the seventh she was allowed in a wheel chair. She began to walk on the eighth day and was dismissed from the hospital on the tenth day, the wound being well healed.

There has been no recurrence of the vaginal bleeding in the past year. Eight months after operation she was readmitted to the service with an incarcerated umbilical hernia which was repaired by Dr. M. L. Parker under local anesthesia and which was followed by an uneventful convalescence.

Whether in this instance the obesity, with slight cardiac decompensation, caused venous congestion of the pedicle as part of generalized congestion, and whether this played a rôle in the causation of the torsion, are questions that cannot be answered definitely, though we feel the relation cannot be disregarded.

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HEMATOSALPINX DUE TO TORSION OF A HYDROSALPINX

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CHARLES OLIM, M.D., SHEFFIELD, ALA.

(From the Surgical Service of Michael Reese Hospital)

TWISTING of the pedicle of a hydrosalpinx causing hematosalpinx and gangrene is uncommon. The following case report of its occurrence in a woman weighing at least 350 pounds, who made an uneventful recovery after operation, seems worthy of record.

There were 35 authentic cases of this condition reported prior to 1900.^{1, 2} Anspach³ tabulated 62 instances of torsion of hydrosalpinx among 87 cases of torsion of tubal enlargement that he reviewed in 1912. Eastman² revised this number to 65, added 3 of his own, and collected an estimated total of 91 cases before 1927. Since that time there have been reported 12 instances of this complication.⁴⁻¹⁵ These, plus the case we report, make a total of at least 104 cases to this date. The figure given is low, as without much question there have been numerous single cases unreported.

Mrs. M. B., aged forty-seven years, was admitted to the Surgical Service of Michael Reese Hospital at 1:00 P.M. on July 6, 1925. Three days previously she began to have dull right lower quadrant abdominal pain, radiating around to the back and down to the symphysis pubis. This remained constant until the evening of July 5, when it became much more severe and intermittent. She became nauseated, but did not vomit. The pain persisted all night, preventing sleep. She was seen by a relief doctor in the morning who gave her a hypodermic, probably morphine, and sent her to the hospital. There was no story of any previous similar attacks.

Past and family history was unessential. Systemic inventory disclosed dyspnea on exertion, marked in climbing stairs, and palpitation and tachycardia. Being up and about for any length of time caused marked edema of the ankles.

Menstruation started at the age of twelve and was always regular. Menopause occurred at forty-two years of age, with no flow until the past few months when she flowed slightly for a day or so at irregular intervals.

Physical examination revealed a markedly obese female, who admitted weighing over 350 pounds, lying comfortably in bed and complaining of no pain. Temperature was 98.2° F. by mouth, pulse rate 100, and respiration 24.

There was slight enlargement of the heart to the left, and a soft systolic blow over the base. The lungs were hyperresonant throughout, with a few râles at the bases. The abdomen was tremendously obese. What seemed to be the liver edge was palpated about one inch below the right costal arch. An umbilical hernia, the size of an orange, was easily reducible. Attempts at determination of rigidity were futile. There was tenderness on deep palpation over the right lower quadrant. Varicosities of both legs were marked. Pelvic examination was most difficult; there was a questionable feeling of fullness and some tenderness in the right side, but nothing definite could be made out. Urinalysis showed one-plus albumin, no sugar. Microscopic examination showed no abnormalities. Leucocyte count was 14,000.

Because of the opiate and the obesity it was difficult to evaluate the symptomatology and physical findings. With a tentative diagnosis of mild acute appendicitis, we decided to observe the patient for several hours.

Examination under anesthesia on Feb. 10, 1937, revealed a normal-sized vaginal opening, the healing of which had progressed by primary intention. The vagina was of ordinary depth and there were no adhesions. The patient was discharged from the hospital Feb. 27, 1937, at which time the vagina was healed and appeared normal and the patient was voiding with control.

The fourth admission of the patient to St. Luke's Hospital was on June 10, 1937. The vaginal orifice had contracted so that it admitted only a number 12 F. sound. Under anesthesia the vagina was dilated to a number 30 F. Exploration of the



Fig. 1.

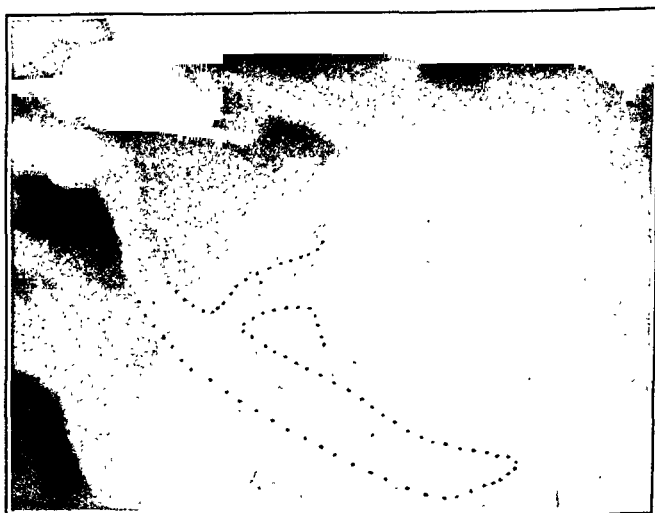


Fig. 2.

vagina at this time disclosed a normal, well-healed mucosa and a vagina of normal depth. The child was discharged as cured June 12, 1937. The vagina was found to be of normal depth and adequate caliber when examined on Nov. 1, 1937.

DISCUSSION

Pseudohermaphroditic changes similar to those found in this patient have been experimentally produced in the female rat by Greene and Ivy.¹ Some of their animals had a hypospadiac penislike external organ identical to that noted in this

PSEUDOHERMAPHRODISM*

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THE patient, aged four and one-half years, was admitted to the Genito-Urinary Service of Dr. Harry Culver, St. Luke's Hospital, Chicago, Illinois on Sept. 24, 1936, with these diagnoses: bilateral undescended testes, hypospadias, precocious physical development, and aene vulgaris.

The history as given by the parents is as follows: The child was born prematurely at seven months and during the first year of life was considered a female. During the second year, however, the child was thought to be a male because of a rapidly developing penis. This enlargement continued during the third and fourth years of life. Because the testes failed to descend, the child at the age of three and one-half years was given injections of antuitrin-S for a period of a year. Coincident with the injections of the antuitrin-S there was a rapid growth of pubic hair but the testes failed to descend.

Examination on Sept. 24, 1936, revealed a four-and-one-half-year-old child with a large, well-developed, muscular body weighing 67 pounds. An extensive aene involved the face. Examination of the external genitalia revealed a penislike structure 4 cm. long at the base of which there was an external urethral orifice. There was a scrotallike structure void of testes which was divided by a shallow cleft and resembled labia majora. Covering the pubic and perineal regions, there was an extensive growth of hair (Fig. 1).

Cystoscopic examination done on Oct. 19, 1936, at St. Luke's Hospital by Dr. Harry Culver revealed an opening in the floor of the urethra two-thirds of the distance out from the bladder neck. This opening, 1.5 cm. in diameter, was partially covered with a delicate membrane. The cystoscope was passed through this opening and a vagina void of an external opening was observed. In the vault of the vagina there was a normal cervix. With a catheter in the anterior portion of the urethra a cystogram was made which demonstrated the urethra, the vagina, the above described communication between the two, and the normal urinary bladder (Fig. 2). Abdominal exploration done at this time revealed normal internal female pelvic organs. X-ray examination demonstrated that the sella was normal. The epinephrine curve was normal. The Aschheim-Zondek test was negative.

From the history, the examination, and the operative findings, it was determined that the patient was a girl with normal uterus, tubes, and ovaries. The external genitalia varied from normal in that the vagina had no external opening but rather opened into the urethra. The thin, delicate membrane covering this vaginal opening was considered to be the hymen. The clitoris resembling a penis was markedly hypertrophied. The patient was discharged from the hospital on Oct. 20, 1936.

The patient was admitted to St. Luke's Hospital the second time on Jan. 18, 1937. On Jan. 25, 1937, the hypertrophied clitoris was amputated and through a medial perineal incision an external opening of the vagina was constructed. The urethro-vaginal communication was closed. An indwelling catheter was placed in the bladder and the vagina was packed with vaseline gauze. The postoperative course was uneventful.

*Presented at a meeting of the Chicago Gynecological Society, March 19, 1937.

In cases of transverse or semilunar incision, the upper uterine flap should be gently retracted upwards with one or two retractors while the head is being delivered by firmly pulling the handle upward in a continuous traction towards the ceiling and with a slight inclination toward the fundus so as to deliver first the lower pole of the head. The extraction of the head is greatly facilitated if at the same time that the operator lifts up the head, the assistant pushes the fundus downwards. Once the head is extracted, the shoulders and the rest of the body are delivered as in other forms of lower cesarean section.



Fig. 1.—Anterior and posterior blades of Acosta-Sison's forceps. The posterior or main blade is the essential part of the instrument. It alone may suffice to extract the head.



Fig. 2.—Acosta-Sison's forceps when both blades are articulated.

The advantages of the instrument when the indications are observed, are as follows:

1. It is not necessary to turn the face of the child and therefore it is time saving.
2. It is the most practical instrument to be used in cases of placenta previa where the head is high.
3. It can be used when the uterine incision is longitudinal but of specific advantage when the incision is transverse semilunar or T-shaped.

patient. Some animals had a normal upper vagina which had no external opening, but opened into the floor of the urethra in a manner similar to that shown in Fig. 2. These workers produced the abnormalities in the offspring by injecting the pregnant mothers with testosterone.

The striking similarity of the findings in the patient presented and those experimentally produced in the rat would indicate that in the human being there was a failure in the development of the sinovaginal bulbs² from which the lower part of the vagina is normally derived. Such a failure in development is undoubtedly the result of masculinization of the urogenital sinus.

Since androgenic substance is found in normal human pregnant urine³ and in placentae,³ it is possible that the human pseudohermaphrodite is produced by an excess of this substance in the maternal fetal organism.

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FORCEPS FOR THE FLOATING HEAD IN LOW CESAREAN SECTION

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(From the Department of Obstetrics, College of Medicine, U. P.)

THIS instrument has been specifically devised for the purpose of delivering the head in situ through a lower uterine segment transverse incision. However, it can be used to extract the head through any form of uterine incision, provided the lower angle of the incision is near the lower pole of the head and provided the head is not engaged.

The instrument is composed of two blades: a posterior one possessing a large deep cephalic curve and an anterior straight blade. The posterior blade is the important part of the instrument and, in most instances, it alone suffices to enucleate and extract the head. The anterior blade is merely accessory and serves when used to steady the hold on the head. It is seldom necessary.

The purpose of the instrument is to extract the head by scooping it out from its bed. This is done by the main blade whose concavity is shaped to accommodate the head and face in their lowermost and posterior portions.

The indications for its use are as follows:

1. The head must be the presenting part.
2. The head must not be engaged but be well above the inlet.
3. The uterine incision must be long enough to allow the passage of the head. The lower part of the uterine incision should correspond to the lower part of the head at about the level of the anterior parietal prominence. Then, facing the feet of the patient, the operator with his left hand guides the insertion of the main blade by gently lifting the head upwards toward the fundus and at the same time with his right hand, he slips the tip of the blade over and closely hugging the cranium and posterior cheek of the fetus. When in place, the handle should be perpendicular to the floor.

craniotomy. This failed, however, because several pieces of the fetal skull became detached, and it was impossible to grasp, crush, and deliver the entire head through the partly dilated cervix. The cervix was dilated manually, and the macerated fetus, weighing 4 pounds and 2 ounces, was delivered by version and breech extraction. This form of delivery, while contraindicated by the presence of infection, was resorted to because it was the one only other possible way of delivering this patient expeditiously. Frank, greenish yellow pus was present on the amniotic surface of the membranes, but not in the uterine cavity. Nonhemolytic streptococci and staphylococci were obtained on culture of this pus.

The patient made an uneventful recovery and was discharged on May 17, 1932.

This case is reported for three reasons: First, because we have not been able to find any case of spontaneous intrauterine separation of the fetal scalp reported in the literature. Second, the importance of certainty of rupture of membranes in patients who give suggestive histories so that such patients may be adequately hospitalized and treated prophylactically. Third, premature rupture of membranes predisposes not only the mother to infection and complications of labor, but her unborn child as well.

51 EAST 90TH STREET

STRANGULATION OF THE FALLOPIAN TUBE

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(From the Queen's Hospital)

THE patient was operated upon by us under the mistaken diagnosis of a probable gangrenous or ruptured appendix:

M. M., an unmarried schoolgirl, aged sixteen, Hawaiian-Caucasian, was admitted as an acute emergency to Queen's Hospital, at 9:30 the evening of April 24, 1936. Chief complaints were nausea, vomiting, and right lower abdominal pain. Marked constipation was present and there was a heavy feeling over the entire lower abdomen for two days before admission. At about this time, a normal menstrual period began. Seven and a half hours before admission the patient had eaten a meal of chop suey. Two hours and thirty minutes after that, she had attacks of cramplike pain around the umbilicus. She vomited almost simultaneously, first the recently ingested food, then greenish fluid. Nausea and vomiting then gave way to retching which continued until the time of admission, at which time the patient raised only small amounts of red-streaked mucus. Three or four semiliquid stools were passed shortly after the onset of the pain. These were believed to be due to a proprietary cathartic which the patient had taken earlier in the day.

There is nothing of note in the patient's past history except that she was kept under observation for two or three days just a year previously for a suspected sub-acute appendicitis. A dull nagging ache and constipation were present and cleared up promptly under small repeated doses of caroids and bile salts. The blood count was normal at that time. Menses commenced at thirteen and have been regular with a minimum of discomfort. Tonsils were taken out under local anesthesia two weeks before the present illness. Convalescence was uneventful. The patient is one of 10 healthy children, and her parents are living and well.

Positive physical findings were as follows: An acutely ill part Hawaiian girl, retching, and complaining of severe pain in the right lower abdomen. Temp. 99.6° F.

Contraindications.—1. It should not be used when the head is partially engaged unless it is possible to disengage the head and bring its lower portion to the lower angle of the uterine incision. In prolonged labors where marked caput succedaneum has been formed, it should not be employed.

The reasons for this are that in such cases, the blade cannot be inserted between the lower part of the head and the uterus.

2. It should not be employed when the bladder attachment is so high that the uterine incision cannot be made over the head unless the bladder can be well dissected off. Other technique must be employed in extracting the fetus in these conditions.

Technique.—1. The patient should be in the Trendelenburg position and the head should be pushed well above the pelvic brim. The same precautions and care are observed as in any low cesarean section as far as the exposure of the lower uterine segment and suctioning off the spill. However no pituitrin or pitocin should be injected until after the posterior or main blade has been inserted in place.

2. The lower angle or portion of the uterine incision (be it longitudinal, transverse semilunar, or T-shaped) should be near the lower pole of the head at about the level of the parietal prominence.

1002 TAFT AVENUE

AN INTRAUTERINE SEPARATION OF FETAL SCALP

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(From the Obstetrical Service of the Harlem Hospital)

MRS. E. A., aged twenty-four years, a colored hospital maid, was first admitted to the Obstetrical Service of the Harlem Hospital on April 23, 1932. Her previous history was negative except for one stillbirth and one miscarriage. Her last menstrual period took place on Sept. 8, 1931. The patient stated that the membranes had ruptured shortly before admission and that labor pains were occurring at intervals of thirty minutes.

The cervix admitted one finger, membranes being intact, felt between examining finger and presenting part. The fetal heart was heard in the left lower quadrant; the rate was 130. Fetal movements were felt. As the pains ceased and the patient wished to return home, she was discharged on April 27 with a diagnosis of false labor and was referred to the Antepartum Clinic for further observation.

The patient was readmitted to the Hospital on May 2; she complained of more frequent labor pains and of the passage of bloody fluid, but no clots, from the vagina. There was no history of trauma, headache, vomiting, chills, or fever. On examination, the cervix admitted one finger. The uterus was the size of a seven months' pregnancy. The fetus was presenting as a vertex in the right occipito-anterior position; the fetal heart could not be heard. The patient's temperature and pulse were normal; her general condition was considered good. Blood Wassermann and Kahn tests were both negative. Vaginal smear showed many gonococci.

On May 4, eleven days after the first admission, a hair-covered piece of fetal scalp about 7 cm. in diameter passed through the vagina. Sharp spicules of bone could be felt within the cervix, which at that time admitted four fingers. With the patient under ether anesthesia, an attempt was made to remove the fetus by

SUMMARY

A case of torsion of two pedunculated hydatids of Morgagni (vesicular appendages), is reported in which the symptoms were such as to lead to the diagnosis of a rupture or gangrene of the appendix. Laparotomy was performed and the right tube was found to be strangulated in its distal portion by the above mentioned cystic bodies. A peculiar series of twists was present, the mechanism of which was not clear. The available literature was carefully reviewed and it was found that seven other similar cases have been previously reported, all of them being young married women or adolescent girls. All cases showed acute abdominal symptomatology urgent enough to demand surgical intervention, and all recovered. Five out of the eight cases were diagnosed as acute appendicitis. Six out of 8 (75 per cent) occurred in the right lower abdomen. A ninth case reported by Meigs, details lacking, is also mentioned.

DISGERMINOMA OVARIUM

SIMON BRODY, M.D., BROOKLYN, N. Y.

(From the Department of Gynecology of the Beth Moses Hospital)

UNTIL recently, these tumors were diagnosed as ovarian carcinomata or sarcomata, and it is only lately that they are properly classified. Most authorities agree that disgerminoma is but mildly malignant. The prognosis seems to be favorable especially if the neoplasm is removed early. The possibility of its presence should be suspected upon finding a solitary solid ovarian neoplasm in a young woman. Conservatism should be the rule, and only the affected ovary should be removed. This point should be borne in mind when the remaining ovary becomes enlarged subsequently, so that conservatism may be practiced whenever possible. The case here reported will bear out this point.

Mrs. L. J., aged twenty-four, white, was admitted to the Beth Moses Hospital, Oct. 27, 1931, complaining of pain in the lower abdomen of two months' duration. Family history was negative. Past personal history was negative. Menstruation started at the age of thirteen. It occurred regularly every twenty-eight days and lasted for four days. There was no dysmenorrhea. Last menstrual period was three weeks before admission; it was regular as to time and duration. Patient had had one child, now three and one-half years old. Physical examination revealed a well-nourished, white woman, not acutely ill. Head, neck, heart, and lungs were essentially negative. Abdomen was soft and not distended. There was tenderness upon deep pressure over the right lower quadrant, where a mass, apparently arising from the pelvis, could be palpated. Vaginal examination showed moderately relaxed introitus; no rectocele or cystocele. The cervix was closed, somewhat eroded. It could be moved from side to side without eliciting any pain. The uterus was normal in size, pushed over to the left by a semisolid mass the size of a small grapefruit, and could be felt through the right fornix. The mass was movable and very tender. A diagnosis of ovarian cyst was made. Blood pressure was 112/80. An examination of the urine and blood did not reveal any abnormal findings. A laparotomy was performed on Oct. 28, 1931. The following findings were noted: Right ovarian tumor, the size of a grapefruit, irregular and nodular in outline. The uterus, left tube and ovary were apparently normal. A right salpingo-oophorectomy was performed. The abdomen was closed without drainage.

Tongue furred and white. Lips dry and cracked. Abdomen moderately distended. Definite tenseness of lower right rectus with tenderness over McBurney's point, and just below it. Decreased peristalsis in the ileocecal region. Hymen intact. No leucorrhœa. Tenderness in right fornix on rectal examination.

The patient was admitted as an emergency to Queen's Hospital where a leucocyte count of 21,000 with 84 per cent of neutrophils was obtained. Hemoglobin was 95 per cent, and the urine was negative except for a trace of albumin.

Eight hours after the onset of the first symptoms, the abdomen was opened through a low right rectus incision. There was a moderate amount of pink-tinged free fluid in the pelvis. The appendix appeared grossly normal. The uterus was very small and infantile. Both ovaries were slender and elongated and appeared otherwise normal. The left tube was normal except for three small pedunculated excrescences just mesial to the fimbriated end. These structures hung like minute

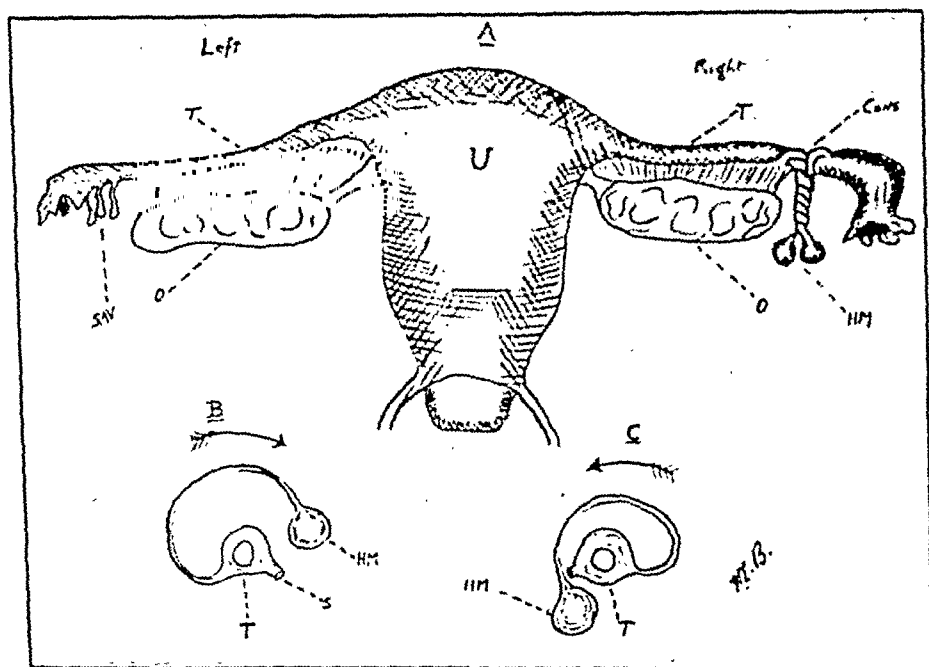


Fig. 1.—A: U, uterus; T, Fallopian tube; O, ovary; SAV, small appendices vesiculosi; HM, stalked hydatids of Morgagni; Cons., constriction produced by the twisted hydatids. B: T, Fallopian tube; HM, hydatid of Morgagni; S, stump showing attachment of stalked hydatid of the opposite side. C: Same lettering as B.

grapes on pedicles of about 2 mm. length. These were removed. The right tube showed no evidence of infection, but its distal end was swollen and cyanotic, and at the junction of the distal 1/3 with the mesial 2/3, there was a tight constricting band produced by the pedicles of two grape-sized cysts filled with clear watery fluid. One of these arose from each side of the right tube and passed up and over and down on the opposite side from which it arose. In addition these sessile pedunculated cysts were twisted on each other so as to make three complete turns. They were untwisted in a counterclockwise manner, and the stalks were severed and ligated at their bases. There was no evidence of any necrosis or stricture, and the tube was left alone. The cyanosis began to clear as soon as the constriction was removed. No other abnormalities were found. The appendix was removed by the usual routine, and the abdomen closed without drainage. Convalescence was uneventful. The patient has had no further recurrence of symptoms, and has menstruated normally and without pain.

a panhysterectomy was performed at the Beth Israel Hospital during March, 1935. The pathologic report was that of a normal uterus and a chronic salpingo-oophoritis. There was no evidence of malignancy in the ovary.

Had the diagnosis of dysgerminoma been known at the time of the patient's second admission to the Hospital, she might have been spared the radical operation, since this tumor is not very malignant, especially when removed early. The patient would have been either treated expectantly, being watched for any further enlargement of the ovary or a biopsy and frozen section examination would have been made at time of operation and the ovary saved.

THREE CASES OF CARCINOMA OF THE CERVIX WITH PROCIDENTIA

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DECUBITUS ulcers very frequently complicate the prolapsed cervical and vaginal mucous membranes, but true carcinoma in association with procidentia, is rarely seen. In fact, whereas about 3 per cent of women develop carcinoma of the normally placed cervix, only one-half of 1 per cent of those with procidentia show this complication.

A review of the literature shows some 50 cases of carcinoma of the cervix with procidentia on record. In 1882 Fritsch, writing in Billroth and Pitla's *Handbuch*, states "it is remarkable that the prolapsed uterus seems to be almost immune against cancer." Judd, of the Mayo Clinic, reports but 3 cases of cervical cancer in 2,188 cases of procidentia. In 1930, a questionnaire sent to leading American gynecologists, revealed the fact that 52.3 per cent of them had never seen a case, while another 27 per cent had seen only one. Sellheim, of Leipzig, Hartmann of Paris, and Schroeder of Kiel, in 1931, had not seen the two conditions associated. Emmert and Taussig, on the other hand, in a fairly recent article, state their belief that if all decubitus ulcers were carefully sectioned and studied pathologically, carcinoma would be found more frequently. This conclusion is based on the fact, that in 10 consecutive uteri removed for procidentia, carcinoma was found four times. In reviewing 683 cases of procidentia, Smith, Graves and Pemberton, found only one case of cancer, and every cervix in the series was carefully studied microscopically. Graves says, "despite the pregnancies, the instrumental labors, the irritations; despite the leucoplakia, hypertrophy, impaired circulation and infection, conditions which predispose to cancer in the normally located cervix, only one patient was found with cancer of the protruding cervix." This seems to prove conclusively, the comparative rarity of carcinoma with procidentia.

In the past ten years, there have been 3 such cases, in the two large English-speaking hospitals of Montreal. These 3 cases illustrate two definite types of cancer, the one a slowly-growing mature form which developed on a cornified cervix which had been prolapsed for years; and the other an immature, highly malignant type developing on a recent prolapse, in a younger woman.

The first of our cases was a woman of seventy-two years, admitted because of a prolapse which she had had for twenty-five years. About the cervical os, was a roughened heaped-up area which bled slightly on being touched. Due to many years of irritation and exposure, the mucous membrane had become markedly thickened,

The pathologic diagnosis at the time was primary medullary carcinoma of the right ovary. Only recently, in reviewing the specimen, the diagnosis of disgerminoma was made, with the following pathologic description:

Gross.—Specimen consisted of an ovarian mass, measuring 12 by 9 by 5 cm., fairly soft in consistency. Its outer surface was nodular, pinkish yellow, with numerous fairly large vessels coursing immediately below the surface. On cross-section the mass consisted of soft, yellowish, nodular tissue, the nodules projecting somewhat above the cut surface and demarcated by narrow fibrous bands.

Microscopic.—The mass was composed of interlacing plaques and nests of polygonal cells with a dustlike or powdery cytoplasm and nuclei that varied considerably in size and tinctorial capacity. The latter varied from small pyknotic to large hyperchromatic nuclei with coarse chromatin clumps and an occasional nucleolus. Numerous mitotic figures were present. The nuclear and cellular membranes were distinct. The cellular masses were enclosed within a trabecular network of fibrillar connective tissue containing many small lymphocytic cells.

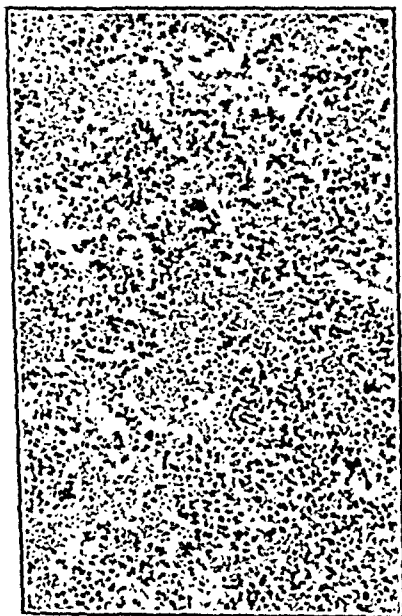


Fig. 1.

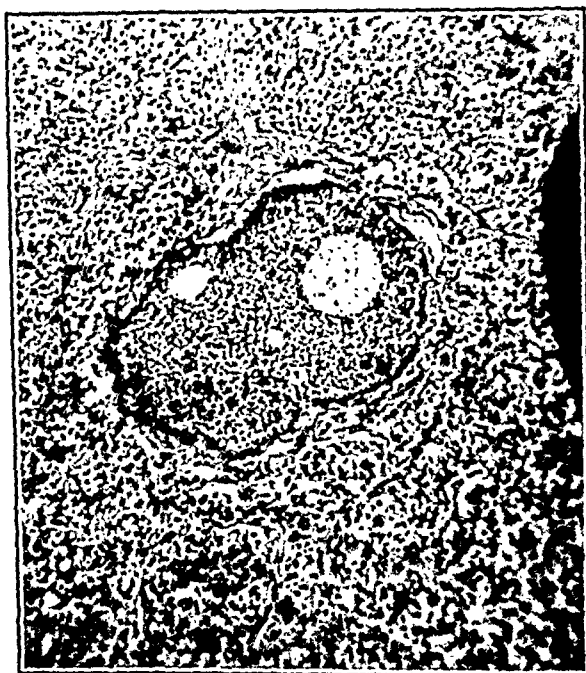


Fig. 2.

Fig. 1.—Interlacing plaques of polygonal cells and trabecular network of connective tissue containing small lymphocytic cells.

Fig. 2.—Follicle, containing ovum, zona pellucida and granulosa cells found in the midst of tumor mass.

While no remnants of ovarian stroma could be distinguished, two ova containing follicles had been found. The ovum, zona pellucida, and granulosa cells were present. In one follicle there was beginning cavity formation. The internal and external thecae could not be found.

Diagnosis.—Disgerminoma ovarii.

The patient made an uneventful recovery. She was discharged from the hospital Nov. 9, 1931, in good condition. She was in good health until February, 1935, at which time she began to complain of pain in the lower abdomen. There was no menstrual disturbance. A vaginal examination showed a slight enlargement of the left ovary. Since the diagnosis of medullary carcinoma of the right ovary was made four years previously, a secondary involvement of the left ovary was suspected, and

Autopsy Findings.—When the abdomen was opened, the uterine vein on the right side, viewed in situ, contained an abundance of air. There were no important gross changes in the aorta or other large vessels of the trunk other than that the inferior vena cava contained an abundance of gas bubbles. The main portion of the pulmonary artery contained only fluid blood mixed with bubbles and no clotted blood.

The entire uterus with Fallopian tubes, ovaries, and liberal portions of the broad ligaments and vagina were removed in toto. The vagina was fastened to an air hose and air was forced into the vagina and uterus under very slight pressure. The uterus became slightly distended; and as air insufflation continued beyond this point, air escaped liberally from a small vein on the right side which apparently had extended to the plexuses of veins in the broad ligaments. It was noteworthy that no air escaped from the Fallopian tubes at this low pressure but flowed freely through the sectioned vein in preference.

The air insufflation was stopped, and a solution of methylene blue was injected through the cut end of the vein where the air escaped. Afterward, the uterus was sectioned and the pathway of the methylene blue could be traced in the fundus of the uterus from serosa to lining along a devious pathway through the muscle. No large channel as such could be demonstrated in the muscle tissue. The Fallopian tubes are anatomically patent.

Anatomic Diagnosis.—Extensive air embolism of the right ovarian vein, superior vena cava, and right heart chambers; and involution of the uterus.

418 MEDICAL-DENTAL BUILDING

OMENTAL ABSCESS FOLLOWING CATHETER PERFORATION OF UTERUS

MORRIS FELLMAN, M.D., JERSEY CITY, N. J.

(From the Jersey City Medical Center)

THE bizarre mechanism by which the peritoneal cavity disposes of foreign bodies is difficult to interpret, because in no two cases can the end-result be predicted with certainty. In one a fulminating peritonitis may develop with toxemia and fatality; another may show a persistent sinus with an opening anywhere in the abdominal wall or through the rectum or vagina; finally encapsulation may take place. The case reported here is of interest because it affords opportunity for speculation concerning the process that goes on when a foreign body reaches the peritoneum through an unsurgical approach. In this instance, a catheter introduced into the uterus for the purpose of criminal abortion was completely passed through it into the abdominal cavity and was later found encapsulated by the greater omentum in which it had caused the formation of a localized abscess.

T. D., aged thirty-two, married, white. Three months after last menstrual period, the patient passed a catheter into the uterus. She stated that she started to bleed at once. This continued for several days and then she passed some tissue by vagina while straining during a bowel movement. Shortly afterward she began to complain of lower abdominal pain and during the day felt chilly and feverish. These were the symptoms for which she was admitted to the Jersey City Medical Center.

She was hospitalized for a period of six days during which she was very much improved. Pelvic examination revealed a laceration and erosion of the cervix of

more like a skin surface than true mucosa. However, even this keratinized epithelium, in this cancer susceptible patient, finally forsook its bounds, for a biopsy showed a low grade malignancy. There has been no recurrence of the growth following a vaginal hysterectomy done eight years ago.

The second case, a woman eighty years of age, was admitted to the Montreal General Hospital in September, 1936, with a complete procidentia which she had had for forty years. Recently there had been some bleeding and purulent discharge. The cervix was very large, about the size of a tangerine, covered with a rough, irregular, crusty growth which sharply demarcated it from the vaginal epithelium. There was slight oozing in several places. A section taken from this mass, just below its junction with the more healthy vaginal epithelium, showed marked prolongations of the epithelium into the tunica propria, a Type 1 carcinoma. A vaginal hysterectomy was done, on October 21, last, and the patient was discharged on November 15, well.

In 1934, a patient admitted to the Royal Victoria Hospital, showed a complete prolapse with a large, friable, fungating cauliflower mass, evidently carcinomatous, attached to the cervix. Under anesthesia the uterus could be replaced in the vagina. This was done and radium placed against the growth in the usual manner, giving a total dosage of 5,440 mg. hr. in three treatments. Neither the carcinoma nor the procidentia has recurred since the treatment.

AIR EMBOLISM

JAMES E. STROH, M.D., AND M. T. OLINGER, M.D., SEATTLE, WASH.

A THIRTY-NINE-YEAR-OLD white woman (para ix) entered the hospital twelve days past the calculated term of pregnancy. All previous nine pregnancies had been full term with no complications. The first (1923) had been a forceps delivery with episiotomy. The other deliveries were spontaneous and normal, the last occurring in October, 1934. The present pregnancy had been uncomplicated clinically, with normal urine and blood pressure.

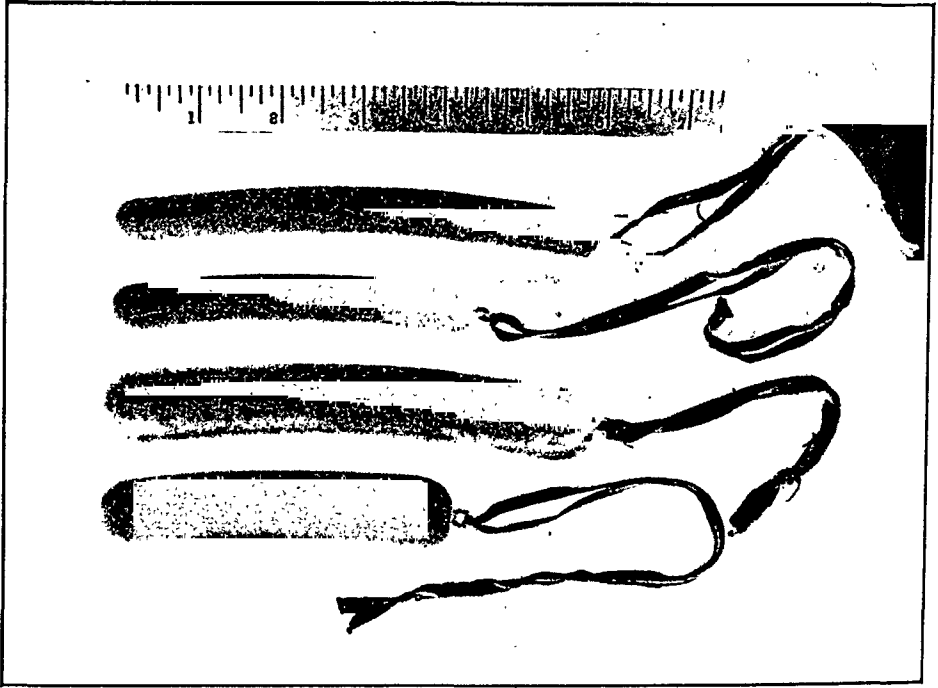
On entry the uterine contractions were irregular. The head was well down on the perineum but there was no cervical dilatation. After being in the hospital for ten or fifteen hours, the uterine contractions ceased altogether. A Watson induction was done and the patient began active labor and delivered forthwith. This was a normal spontaneous delivery with an estimated blood loss of about 100 c.c.

The postpartum period was uneventful, until on the morning of the seventh day when shortly after assuming the knee-chest position for the first time, the patient suddenly collapsed and became unconscious. There was cyanosis of the lips and fingernail beds. The head was pulled to the right with the eyes turned in the same direction. Pupils dilated, the neck was stiff, and the arms and legs spastic. Respiration was forceful and increased in rate. The radial pulse was imperceptible. On examination of the chest there was no dullness on percussion, no râles nor friction rubs. Breath sounds were normal, pulse 88, heart rhythmical and tones of fairly good quality. No murmurs or other unusual sounds were heard.

One ampule of coramine was given intravenously and 1 c.c. of adrenalin subcutaneously. Artificial respiration was used. In spite of this the patient ceased breathing and died quite suddenly, not more than four or five minutes from the time of the onset.

out of the rectum and contaminate the field, as so often happens when a sponge stick is used as a rectal guide. It is preferable to the finger in the rectum because it allows the operator the use of both hands and minimizes the opportunities for infection.

The guides or indicators I have been using are made of aluminum and have the following dimensions: $4\frac{1}{2}$ by 3 inches; $4\frac{1}{2}$ by 2 inches; 6 by 3 inches; 6 by 2 inches. Other metals or rubber may be used instead of aluminum.



In the majority of cases I use the $4\frac{1}{2}$ by 3 inch guide; where the anal canal is smaller, the $4\frac{1}{2}$ by 2 inch. In cases of sphincter tears I employ the larger guides.

The guides are lubricated with sterile soap or sterile lubricating jelly. The eye end is grasped by a sponge holder or uterine dressing forceps and the guide is gently introduced into the rectum. The sterile tapes are left dangling outside the rectum and at the completion of the repair, the guide is easily removed by pulling on the tapes.

1882 GRAND CONCOURSE

Politzer, G.: Abnormally Short Umbilical Cord and Its Consequences, Wien. Klin. Wchnschr. 49: 40, 1936.

The author describes a human embryo between 7 and 8 mm. in length in which there is a 90 degree rotation of the embryonic axis to the left. The facial anlage is in contact with the left "rump." The author attributes this torsion to an abnormally short umbilical cord. This condition is normal in the chick embryo and with embryonic development at maturity corrects itself with no evil consequences. Two theoretical possibilities are cited for this embryo; it may have corrected itself by subsequent growth or it could have persisted and then become responsible for a congenital torsion of the skeleton resulting in scoliosis.

W. B. SERBIN.

moderate degree, very slight tenderness in the fornices and no bleeding. There was only a small amount of brownish yellow cervical discharge. Abdominal examination was negative. It was noteworthy that she failed to recall what happened to the catheter but because of the association of the passage of uterine contents with defecation it was assumed that it also had disappeared at that time.

Twenty days later the patient sought re-admission to the hospital. Since her discharge, she complained of persistent sharp pain in the right lower quadrant, aggravated by standing and walking and slightly improved while lying down. She had occasional attacks of nausea and vomiting. Upon examination there was tenderness in the right lower quadrant over McBurney's point and moderate rigidity. She had no chills or fever during her original stay. The temperature was 100.8° F. and the white blood count showed 10,250 leucocytes with a differential of 76 polys and 24 lymphocytes.

However, it was felt that an acute appendiceal involvement was present and a laparotomy was done. When the peritoneum was incised the omentum was unusually adherent. As it was freed a hard and friable mass was noticed. When it was delivered, a perforation was accidentally made and through this opening a small amount of greenish yellow pus, with a colon odor, was expressed. The opening was further enlarged and the object was discovered, which upon removal and examination was found to be a hard rubber catheter. This had become curled upon itself and tucked within the omental folds. Upon the superior portion of the uterine fundus, near the left tube, a healed perforation, the diameter of which compared to the size of the catheter, was found. This was the point of entrance. The diseased omentum was resected and the pathologic report follows: Section of specimen marked "omental tissue" shows a fibro-adipose vascular stroma infiltrated with polys. Diagnosis: omental abscess.

The bacteriologic report of the abscess showed occasional *Staphylococcus aureus* and many *B. coli*.

For the first few days postoperative the patient had a mildly stormy course associated with distention and nausea. This cleared up and on her eighth day a small infection in the lower angle of the wound developed. She was discharged on her twenty-ninth postoperative day fully healed and recovered.

118 JEWETT AVENUE

A RECTAL GUIDE

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IN REPAIRING lacerations of the perineum following labor, especially if deep bites are taken, occasionally one finds that, inadvertently, the suture material has entered the rectum.

Some claim that this accident is merely an incident and harmless, nevertheless the possibilities of fistula and infection cannot be denied.

I have found that an indicator in the rectum is of value not only in avoiding puncture but also in repairing fresh rectal and sphincter tears and rectovaginal fistulas. The torn sphincter muscles can be more easily identified and approximated over the indicator. During perineoplasty, an indicator also will frequently prove of aid.

I have found that the sausage-shaped device here illustrated fills the requirements. Because of its shape it does not slide and is therefore not likely to slip

Special Article

HENRY MILLER AND THE DEVELOPMENT OF SCIENTIFIC OBSTETRICS IN THE NEW WEST*

HERBERT THOMS, M.D., NEW HAVEN, CONN.

IN THE history of America it is the spirit of the pioneer which stands out as a vital force in that interesting drama. The story of the development of scientific medicine on our shores reveals the same powerful influence and the indomitable Daniel Drake comes to mind as a notable example of this attitude of mind. In the history of American obstetrics, this spirit of the pioneer is shown not only in those hardy souls who braved the Atlantic to receive the torch from the masters in the old world, but also in those who carried the light into the then remote parts of the new world. Such a one was Henry Miller of Louisville, Kentucky, whose influence in the development of obstetrics in the west was unparalleled.

Henry Miller came by his pioneering spirit honestly, for his father was one of the first settlers in Barren County in the Green River section of Kentucky. It was here in the town of Glasgow that he was born Nov. 1, 1800. Henry Miller was denied the advantages of a collegiate training, his education being limited to that afforded by the country schools. In the first edition of his book, he says, "The author's education was not acquired in academic halls, but in the primitive school-houses of his native state and upon the ample sward, shaded by forest trees, appurtenant there unto. So you see he was reared after the fashion of Socrates, imbibing knowledge in the schoolhouse under the shade of the trees, and not infrequently perched upon their boughs."

At the age of seventeen, he began the study of medicine under two local physicians, Drs. Bainbridge and Gist. The practice of these men extended over a wide area, and in the absence of apothecaries they were obliged to compound their own medicines. At that time, much work of this character was relegated to the apprentice in medicine, including the extraction of teeth and the letting of blood. In this capacity the young Miller is said to have been "chief pharmacist, dentist and bleeder for his county." Two years later, in 1819, Henry Miller rode on horseback to Lexington to attend the first full course of lectures in the Medical Department of Transylvania University. Here he joined a student body of less than forty members and remained throughout the course. Partial courses had been given at Transylvania before but at this time a more common organization had been effected. The situation in Kentucky at that time seemed propitious for such an enterprise, the new west was becoming more thickly settled and more young men were turning to the professions. Furthermore, a journey to centers like Philadelphia was not only tedious but possibly dangerous. As late as 1820,

*NOTE: This biographic sketch should prove of interest in view of the Centenary celebration in 1934 which marked the founding of the Louisville Medical School.

INEXPENSIVE OBSTETRIC MANIKINS

PAUL E. HOFFMANN, M.D., SAN FRANCISCO, CALIF.

(From the Department of Obstetrics and Gynecology, Stanford University School of Medicine)

MANIKINS, for obstetric teaching, are expensive, usually requiring an expenditure of about three hundred dollars each. Recently we were confronted with the need for additional manikins, and because of a shortage of funds made an investigation which solved our dilemma. We consulted local artisans about prices for manikins and considered such materials as cast aluminum, plaster, and wood. The latter offered the best possibilities, and a wood carver was consulted. This artisan copied one of our imported models in poplar wood, and for fifty-five dollars each we acquired four excellent manikins weighing no more than those of foreign manufacture.

Other less expensive woods could have been used to reduce the cost still further, but poplar wood seemed an ideal material because of its close grain and its re-

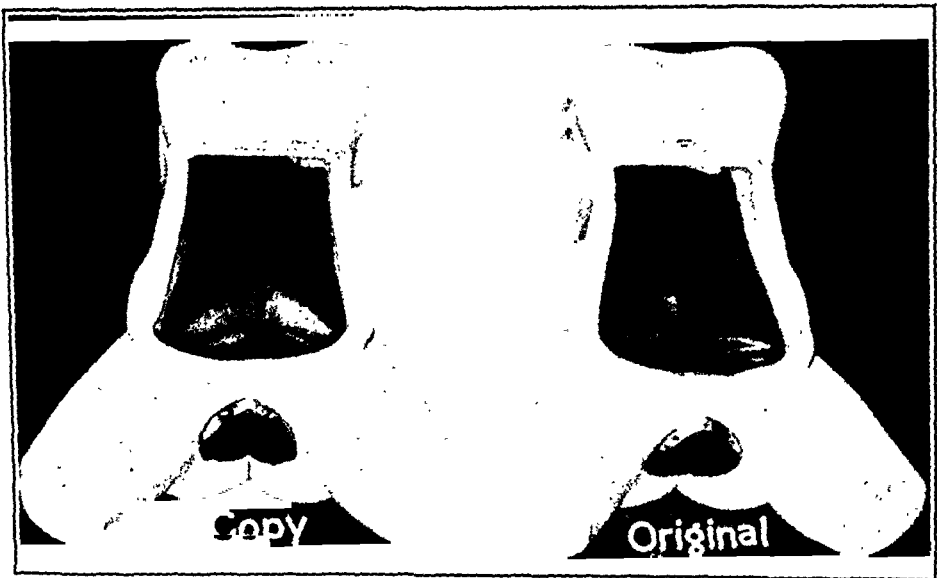


Fig. 1.

sistance to checking. The wood block for each manikin was built up of smaller pieces in order to strengthen the structure and prevent splitting during carving. Sufficient time was allowed to permit the glue to harden well. Otherwise trouble would have been encountered during carving. Four weeks is sufficient if the wood has been properly kiln dried. Each manikin received several coats of hard drying paint of flesh color, applied with a spray gun, following preparation of the wood with boiled linseed oil.

Rubber vulvas similar to those found on the commercial manikins were obtained and fitted on with a metal rim made of brass by a local coppersmith at a small cost, who also made similar fittings for the peritoneal rubber coverings.

These homemade manikins have been in use for three months and have proved satisfactory in every respect. In appearance they cannot be distinguished from the commercial product (Fig. 1) and the total cost for each did not exceed seventy-five dollars.

Because of the great saving and the satisfactory service given by these manikins the teaching staff of this department reports its experience.

Philadelphia, physicians were just beginning the use of cowpox virus. Benjamin W. Dudley in anatomy and surgery had enjoyed the advantages of four years of postgraduate study in Europe and was a renowned lithotomist.

At the end of the course, Henry Miller returned home and was taken into partnership with Bainbridge (Gist having removed to New Castle in Henry County). In the fall of 1821, he returned to Lexington for a second course of lectures, receiving the degree of doctor of medicine the next spring. His thesis, "Relation Between the Sanguiferous and Nervous Systems," was accorded such merit that it was published by the faculty.

A contemporary has left us this description of events following shortly. "At the following session of the Transylvania, the students began to express dissatisfaction with the opportunities afforded them for the study of practical anatomy. This branch of instruction was engrossed by Dr. Dudley, and carried on in the room above his amphitheater. The students procured their subjects as best they could from the graveyards in the city and surrounding country, and performed their dissections with but little supervision by the professor, while they were required to pay a very liberal fee. The complaints of the class were brought before the faculty and they resolved to appoint a demonstrator. Dr. Miller received the appointment and the first intimation he had of the discontent of the class and the establishment of a demonstratorship, was the official notice sent him by the Dean, Professor Richardson." Miller relinquished his practice in Glasgow in order to prepare himself for the new duties and spent some time in study in Philadelphia. On his return he was surprised to learn that Dudley had not given his consent to the appointment. Rather than enter a contest with his former teacher, he withdrew and returned to practice. In 1827, he removed to Harrodsburg in Mercer County, at that time the most popular watering place in the west. For nine years he remained here, building up an extensive practice.

In 1835, Henry Miller was called to Louisville to aid in organizing a medical school there. A number of resident physicians had already obtained a charter and the president of the board of trustees offered him the choice between the chairs of Anatomy, Practice of Medicine, and Obstetrics. He chose the latter and removed to Louisville in the fall of 1835. On his arrival he found the prospects for the new school uncertain, and the project about to be abandoned. He was not to be discouraged, however, and he aroused the community to the importance of the subject by a series of articles in the *Louisville Journal*. So powerful was the appeal that the faculty at Transylvania soon sensed the danger of a rival school at Louisville, a growing city where greater clinical facilities for teaching were possible. As a result, Professors Caldwell, Cooke, and Yandell of that institution joined the Medical Institute of Louisville, which later was merged into the Medical Department of Louisville University. The addition of these well known names brought great prestige to the new school. Caldwell became professor of materia medica; John E. Cooke, professor of theory and practice of medicine, and Lunsford P. Yandell occupied the chair of chemistry and materia medica. Later additions to this faculty included Daniel Drake and Samuel D. Gross. For twenty-one years, despite numerous changes in the faculty, Henry Miller served as professor of obstetrics and diseases

Charles Caldwell recorded that "so deep and adhesive was the mud," that during four days he was able to cover but sixty miles on horseback.

As early as 1792, Transylvania "Seminary" had located in Lexington and in 1799 the Medical Department and Law College were organized. At a later reorganization of the Medical Department, Daniel Drake occupied the chair of Materia Medica and Medical Botany for a short time. The year 1819 saw a rebirth of interest in the Medical College



and the citizens of Lexington, the legislature, and various physicians in the south all pledged money for its development and maintenance. Among the medical faculty at that time were men of outstanding ability. Charles Caldwell, who occupied the chair of the Institutes of Medicine, and noted for his eloquence, had formerly been professor of natural history in the University of Pennsylvania. Samuel Brown in theory and practice, as early as 1802, had shown his pioneering spirit by vaccinating upwards of five hundred persons when at that time in New York and

neering spirit is shown in the championship of specular vaginal examination and the use of anesthetics in labor, both highly controversial subjects at that time. With regard to the former he writes:

“Many writers and among them, Professor Simpson, are particular to direct that the speculum should be introduced under cover and with the aid of the touch alone, and some of them think that it is more decent and less offensive to female modesty, if the patient be placed upon her left side rather than the back. I used to be of this way of thinking, but my thoughts here changed, for after all the genital organs, including the vulva, must be seen; and if they are not seen sursum, they must be seen deorsum, so that it is only a sham to take these delicate precautions. Genuine modesty consists in scrupulously protecting our patients from unnecessary exposure; all beyond this is counterfeit.” Regarding anaesthesia in labor, he records, “It was not until the twentieth of February, 1848, that anaesthetics were used in midwifery in Louisville, or so far as I know on this side of the Allegheny Mountains. The occasion occurred in my own practice,” and again, “Believing that etherization in childbirth is one of the greatest benefactions of science, which has been made in this or any other age, and having enjoyed abundant opportunities of witnessing its triumphs, I should be recreant alike to truth and duty if I did not attempt to vindicate it against the objections which have been alleged by those high authorities in obstetric medicine.” [i.e. Ramsbotham and Meigs.]

As in the previous work, the pathology of pregnancy receives but scant treatment. Once more it is the author's wish to present an “exposition of the cardinal principles of obstetrics,” and again we see excellent chapters on the mechanism of labor and the common obstetric operations of that day. The sound principles inculcated in these fields show ample reason why this textbook had such wide influence in this country, quite beyond the author's own time.

In an age when pomposity and bombast were rife in medicine as in other fields of intellectual endeavor, it is gratifying to turn to the record of the life and work of Henry Miller and to see there in his honest simplicity, his essential greatness. As a prophet he was not without honor in his own country, for in 1859 at a meeting of the American Medical Association in Louisville, he was elected president. His long time friend and colleague, Samuel D. Gross said of him, “He was essentially a strong man, with a well-ordered and philosophical mind. Whatever he knew, he knew well.” I think we must come to the conclusion that the success of Henry Miller as a man was due primarily to his great faith in himself. He was confident of the worth of the work he was doing and with ingenuous sincerity wrote: “Long ago it was said or sung, ‘Westward the star of empire takes its way’ and why may it not have reached the banks of the Ohio by this time?” In the roster of important contributors to the development of scientific obstetrics in America the name of Henry Miller must occupy a lofty position.

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of women and children. In 1858 he resigned in order to devote more attention to his practice and nine years later a special chair of medical and surgical diseases of women was created for him. After a year he resigned this professorship to take a similar one in the Louisville Medical College, which he held until the time of his death, Feb. 8, 1874.

Of Henry Miller the teacher, his colleague Yandell has given us the following description.

"As a lecturer, Dr. Miller rose to distinction in spite of the greatest natural disadvantages. His voice was not good and his delivery was nearly as bad as it could be. It was painful to listen to him, until one had grown accustomed to his manner, so great was his difficulty of utterance, and yet he was a successful teacher. The slowness with which he was obliged to proceed enabled his pupils to take in all his matter, and his thorough mastery of his subject gave weight to his instructions. It was his happy constitution of mind to become so engrossed by the matter of his discourse that the drowsiness of his audience or even disorders in the lecture room were unnoticed, and his good nature contributed to the popularity which he gained by the sound practical character of his lectures. He had both humor and imagination, and would enliven his dry prelections by sallies of wit when his subject invited; but the quality of mind to which he owed his influence among men and his reputation as a teacher and a practitioner, was his sound vigorous understanding."

As a writer he was a frequent contributor to the journals of his day and among his papers is the report of a case of ovariectomy in 1847. His first textbook, *A Theoretical and Practical Treatise on Human Parturition*, appeared in 1849. In the preface he writes, "To give a full, correct and lurid description of the mechanism of labor is the leading object which the author had in view in writing his book," and, "We need at this time, a native authority to educe order out of confusion, and set up a national standard, under which all practitioners may arrange themselves and be cemented by a common bond of union." That the author was able to accomplish much of his desire is witnessed by the work itself.

At that time, the classification and nomenclature of fetal presentations and positions which prevailed in this country was that of Baudelocque made popular by Dewees. Some idea of the complexity and confusion existing in this subject may be gathered from Miller's text, as follows:

"M. Baudelocque's classification embraced *twenty-three genera* of presentations consisting of as many distinct regions of the fetal body, which he supposed might offer at the superior strait. Four of these genera he found at the cephalic and pelvic extremities of the fetus, viz., presentations of the vertex, of the feet, knees and nates, while the four planes of the body, between these extremities, furnished him—the anterior, with the face, the forepart of the neck, the breast, abdomen and thighs (five genera); the posterior, with the occiput, nape of the neck, side of the neck, the shoulder, side of the thorax and the hip (ten genera). These genera include ninety-four species which it would be useless as tedious to enumerate."

The classification which Miller recommended was essentially that proposed by Dugés and one which is largely universal today. To him belongs the credit for its early introduction into the literature of this country. The work is largely concerned with the mechanism of labor and such operative procedures as forceps operations and destructive measures. The pathology of pregnancy is not emphasized.

The second production from Miller's pen was *The Principles and Practice of Obstetrics*, which appeared in 1858. In this work his pio-

in 1919 reported an efficacy of 75 per cent for castor oil and quinine, subsequent observers have been unable to approach this figure even in patients at or beyond term. In 199 attempts at induction with this method reported by Reddoch, there were 100 successes (50.2 per cent). This is approximately the figure obtained by McGoogan. In the reviewer's hands the success of the procedure has been under 35 per cent. There is considerable evidence which suggests that quinine in large doses exerts a harmful effect upon the child. The studies of Sadler, Dilling, and Gemmell show that quinine passes readily into the placenta and amniotic fluid; it has been found in fetal tissues in strengths which are capable of toxic effect and after intervals which suggest that maternal reabsorption from the fetus is slow and that its excretion into the fetal urine is limited. In common with other obstetricians these authors find that the presence of meconium in the amniotic fluid is more common after quinine. While it is impossible to prove statistically that quinine is an actual cause of stillbirth, many obstetricians feel that it is partially responsible for a few such deaths and for this reason the present tendency is to reduce the total dosage to 10 gr. (0.6 gm.) or less. In this connection it is helpful to know that Schübel, on the basis of animal experiments, considers small doses of this drug more efficient in producing uterine contractions than large ones. He points out that quinine is both a stimulant and a depressant of the sympathetic nervous system, depending on the method of administration and dosage; thus, weak solutions of quinine stimulate the isolated rabbit uterus, whereas strong concentrations paralyze it. For this reason alone, he urges that obstetricians use small amounts for the induction of labor and recommends 1 to 2 mg. of quinine hydrochloride intramuscularly for each kilogram of body weight in order to produce uterine contractions in from one to two hours. In a woman weighing 140 pounds this would mean an intramuscular dosage of only 1 to 2 gr. In Schübel's opinion such small quantities sensitize the uterus to mechanical and chemical stimuli for days, especially to posterior pituitary preparations. After minute doses of quinine small amounts of pituitary extract suffice to produce uterine contractions, but if large quantities of quinine are given, the uterus remains paralyzed for many days and does not respond to pituitary preparations. Finally, Schübel shows that in some obstetric clinics where small doses of quinine have been employed, as he has recommended, better results have been obtained than with the large amounts previously used.

Although induction of labor by castor oil and quinine frequently fails, the method possesses the advantage of being harmless, provided the dosage of quinine is limited to 10 gr. (0.6 gm.). Its use should be restricted to patients at or beyond term since it will rarely succeed before then.

When castor oil and quinine, or castor oil alone, are followed by pituitrin, the effectiveness of the procedure is considerably increased, the incidence of success ranging from 50 per cent (Stein and Dover) to 90 per cent (Watson). At the same time a certain degree of risk to the child is introduced since tetanic contraction of the uterus occasionally follows. Efforts have been made to circumvent this danger in two ways: by repeated small doses of pituitrin and by its intranasal application. Mathieu in 1927 recommended a technique which consisted in giving quinine and castor oil, and two hours later a hot enema,

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE INDUCTION OF LABOR

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THE frequency with which labor is being induced today by artificial rupture of the membranes constitutes one of the notable trends in modern obstetrics. When the method was introduced to American obstetricians between 1928 and 1930 by the work of Jackson, Slemmons, and Guttmaacher and Douglas, the reports of these authors met with widespread skepticism. As pointed out by Schumann, it was feared that errors in presentation would follow its use, that an aggravation of the usual injuries to the birth canal would occur, that puerperal infection would often follow and that the fetal mortality would be increased due to prolapse of the cord and other accidents. For almost ten years now the method has been in extensive use with several thousand inductions on record; yet none of these things has happened. On the contrary, several authors state that their maternal morbidity and fetal mortality have actually been reduced following induction by this method; all agree that the average length of labor has been shortened by almost 50 per cent. These gratifying results carry far-reaching implications. They not only challenge our previous conception of "dry labor" but seem to indicate that the major rôle we have long assigned to the bag of waters in cervical dilatation is incorrect. From a practical point of view they have given rise to the impression that labor may be induced safely by this method in almost any type of case, regardless of indication or contraindication. These facts suggest that this widespread practice merits careful evaluation. When compared with other methods, what are its efficacy and safety?

CASTOR OIL, QUININE, AND PITUITRIN

The most widely used medicinal method of induction is *castor oil and quinine*. The rationale of the procedure is based on the belief that the castor oil produces a certain degree of pelvic engorgement which, either directly or through nervous plexuses, stimulates uterine contractions. When the pelvic congestion is at its height, that is, when evacuation occurs, an attempt is made to augment the effect by a hot enema and small doses of quinine. In general, this method has lost favor during recent years because (1) it is successful in less than 50 per cent of cases, even with patients at term and (2) quinine is suspected of exerting a harmful effect on the fetus in any but the smallest doses. Although Reis

ruptured before labor began (in one case a whole month elapsed), while in 102 the rupture occurred at the onset of or early in labor. In 16 patients with membranes ruptured for twenty-four hours or more before the onset of labor, the average duration of labor was some sixteen hours for the 8 primiparae and some seven hours for the 8 multiparae. In the whole group of 182 the average length of labor was thirteen hours forty-two minutes for the primiparae and seven hours forty-two minutes for the multiparae. Quigley, in a study of pregnancy and labor in elderly primiparae (thirty-five years or more), noted dry labor in 82 out of 237 cases. The average length of labor in these patients was 11.6 hours, while in the entire series it was 15.3 hours. One of the most comprehensive and detailed reports on this subject is that by Margaret Schulze on 604 cases of dry labor occurring in a series of 6,500 deliveries (9.3 per cent). She considered only those cases in which rupture of the membranes occurred prior to or at the onset of labor. The length of labor was shorter than the average for the patients with intact membranes, the first stage being chiefly affected. The average of the first stage was 12.1 hours for primiparae and 7.1 hours for multiparae, with second stages averaging 1.82 hours and 0.9 hour, respectively. In 8.4 per cent of the patients labor lasted over twenty-four hours, as contrasted with 12.4 per cent in 500 consecutive cases reported from the same clinic by Slemmons. The recent reports of Sunde and of Wichmann, covering large series of cases observed in Oslo and Helsingfors, show a similar shortening of labor after spontaneous, premature rupture of the membranes. Following artificial rupture of the membranes before the onset of labor, the results are even more striking. In one of the first studies of the procedure, Guttmacher and Douglas in 1931 reported 120 cases of induction by this method and found that labor was shorter than in normal cases by 73 per cent in primiparae and by 116 per cent in multiparae. In primiparae and multiparae alike, both stages were shortened and this could be ascribed only to the rupture of the membranes. Subsequent studies by Slemmons, Morton, A. G. King, Reddoch, Fitzgibbon, Stern, Mathieu and Holman, Plass and others show similar results and afford ample evidence that labor is shortened almost 50 per cent by artificial rupture of the membranes.

But it may be argued that such rapid cervical dilatation is pathologic and must be associated with considerable trauma to the cervix. This contention is refuted by the findings of several authors. For instance, Schumann made careful examinations of the cervix during and after labor and found that patients whose membranes had been ruptured prematurely showed a slightly lower incidence of cervical laceration than those with intact membranes. Similarly, N. H. Williams, whose custom it is to repair the cervix on the ninth day, reports that intermediate repair is decreased some 50 per cent in patients with premature rupture of the membranes.

Premature rupture of the membranes, then, whether spontaneous or artificial, usually accelerates cervical dilatation and does so with no increase of cervical trauma. In view of this fact it would seem illogical to assign to the bag of waters any important rôle in cervical dilatation and little by little the old teaching on this subject is being abandoned. Thus, Slemmons believes that the classical explanation of cervical dilatation by the hydrostatic wedge of the bag of waters is incorrect. Deprived of the possible action of such a mechanism, 132 cases reported

followed by pituitary extract in 3 minim doses intramuscularly at half-hourly intervals for as many as fifteen doses if necessary. In order to take advantage of the oxytocic effect of the pelvic engorgement caused by the castor oil, the quinine and the hot enema, he followed the enema immediately with the first injection of pituitary extract. In 91 patients he had 71 per cent success. Watson's high incidence of success with the method (90 per cent) was achieved by employing much higher dosages of pituitrin than are ordinarily considered safe, namely, 0.5 c.c. injections until six, if necessary, have been given. Impressed by the danger from tetanic contraction of the uterus following pituitrin, Hofbauer in 1927 introduced the nasal administration of the hormone, his idea being that the pituitrin-soaked pledget of cotton could be withdrawn from the nose if uterine contractions became too strong. This method has now been in general use for some ten years and is to be recommended with the following reservations: (1) following the application of the pituitrin, the obstetrician must stay constantly at the bedside, observe the duration of each contraction and count the fetal heart beats thereafter; a contraction which lasts longer than two minutes or a fetal heart rate below 100 calls for withdrawal of the pituitrin-soaked pledget; (2) failure to induce contractions is sometimes observed as the result of faulty absorption, due apparently to some abnormality of the turbinate mucous membrane. Such a failure does not rule out idiosyncrasy (as some authors suggest), and if recourse must be had to intramuscular pituitrin, the usual caution must be exercised, that is, the maximal dose should be three minims. Pituitrin is contraindicated in the toxemias of pregnancy because of its pressor effect on blood pressure.

ARTIFICIAL RUPTURE OF THE MEMBRANES

It will be recalled that artificial rupture of the membranes, a favorite method of inducing labor in the late eighteenth century, was discarded early in the nineteenth century and for a hundred years or so was little used. The long aversion to the procedure hung on the conviction that the bag of waters played the principal rôle in cervical dilatation and was therefore indispensable to normal labor. This belief rested not only on theoretical considerations but on the observation that cases of spontaneous, premature rupture of the membranes were sometimes followed by prolonged labor and other complications. Emphasized in textbook after textbook, this conception of the bag of waters has long been regarded as an almost axiomatic truth. It has been part and parcel of all our obstetric teaching, and we find it difficult, as did obstetricians a hundred years ago, to view without prejudice the deliberate puncture of the membranes for the induction of labor or any other purpose. Consequently, if we are to make an unbiased appraisal of this procedure, it is necessary at the outset to inquire into the validity of this old doctrine.

If the bag of waters serves an important function in cervical dilatation, it is self-evident that its preservation should shorten labor whereas its rupture should prolong it. The results of recent studies on this subject, covering many thousand cases, have been clear-cut and decisive: premature rupture of the membranes, both in primigravidae and multigravidae, *shortens* the average duration of labor. This holds true whether the rupture has been spontaneous or artificial. For instance, Brodhead has reported 182 private cases, in 80 of which the membranes

conditions constitutes a definite contraindication to the method. Probably the most important contraindication is an unengaged head because of the associated danger of prolapse of the umbilical cord. The very fact that the head is high in a primigravida, moreover, indicates that the patient has probably not yet approached the date when labor may be expected to start spontaneously. (About an 85 per cent probability, since in approximately this proportion of primigravidae the head is engaged during the last week of pregnancy.) This brings us to the second contraindication. The method should never be used if the patient is more than ten days from her expected date of confinement because experience shows that it is less successful at that time; indeed, all methods of induction become less efficacious as they are used further and further from term. The third important contraindication to the method is a long firm cervix. This not only renders the technical puncturing of the membranes difficult but presages a long latent period before labor ensues and, in addition, a prolonged first stage (Table I). Most authors agree that the method is also unsuitable in breech presentations.

The importance of these contraindications to artificial rupture of the membranes is rather generally recognized but recently Plass has induced labor by this method in 681 cases, disregarding entirely two of the contraindications we have mentioned. The presenting part was floating in 335 cases and was fixed but still above the spines in 300 others, leav-

TABLE I. SHOWING THE LATENT PERIOD AND DURATION OF LABOR AS GOVERNED BY THE CONDITION OF THE CERVIX IN 150 CASES OF ARTIFICIAL RUPTURE OF THE MEMBRANES. (MORTON, 1933)

CONDITION OF CERVIX	LATENT PERIOD		DURATION LABOR	
	MULTIP.	PRIMIP.	MULTIP.	PRIMIP.
Canal obliterated, os dilated 1, 2, 3 cm.	0.5 hr.	1.03	2.18	6.26
Cervix partially obliterated, just open	1.06 hr.	1.56	3.72	7.01
Cervix long, closed	5.0 hr.	2.69	4.82	15.85

ing only 46 patients with the head actually engaged. The cervix was completely effaced in only six instances but was thinned to some extent in 42 others, while it was thick and uneffaced in 633. The canal admitted one finger in 468 cases and two fingers in 181 cases, while in 32 instances it was closed, necessitating digital or instrumental dilatation before the amnion could be reached. All but 29 of the patients, however, were at or very near term. In general, the results were surprisingly good with no maternal mortality and an exceedingly low fetal mortality. "There were five prolapsed cords," Plass points out, "a higher incidence than should have been noted if spontaneous rupture of the membranes had been permitted; two of these babies were lost and their deaths may be attributed to the procedure. Prolapse of an arm occurred once and demanded later intervention to accomplish delivery." In a series of 303 cases at the Johns Hopkins Hospital, quite comparable in other respects to those of Plass, but in which the head was engaged, there was only one case of prolapsed cord. This represents an incidence of 0.3 per cent, whereas in Plass' series it was approximately 1 per cent. The importance of Plass' work lies in the demonstration that this method may be employed in exceptional cases, under urgent indication, even though the head is not engaged and the cervix

by him suffered no handicap with regard to the first stage and terminated satisfactorily. Nor did the presenting part of the fetus act as a substitute, for this contingency was ruled out by careful, frequent rectal examinations. He found, moreover, that the phenomena associated with the transformation of the cervix following premature rupture of the membranes were the same as those accepted as normal. First, the canal became effaced with simultaneous obliteration of the internal os; and subsequently the external os became more and more widely dilated. Slemons believes that the mechanism of the first stage of labor from beginning to end may adequately be explained by retraction of the uterus, that is, by rearrangement of the muscle fibers in response to the forces which pull them upward toward the fundus. Similarly, Fitzgibbon of the Rotunda is convinced that "the bag of waters does not play any part in the dilatation of the cervix." Kreis is of the opinion that the bag of waters has little or no effect on the effacement of the cervix or on the dilatation of the external os, but considers these changes due to the action of the longitudinal fibers of the uterus on the fibers of the cervix which are pulled up into the lower segment. E. L. King and other authors agree with these views. In short, the belief is growing, on the basis of sound evidence, that the bag of waters serves no function in cervical dilatation and effacement. As we have indicated, an honest acceptance of this new viewpoint is prerequisite to any fair appraisal of the subject at hand.

Technique.—Rupture of the membranes is accomplished after placing the patient in the lithotomy position and carrying out full antiseptic toilet of the vulva as for delivery. The first two fingers of one hand are inserted into the cervix until the membranes are encountered. The cervix is gently stretched and the membranes stripped from the region of the internal os. A long hook, similar to one blade of a disarticulated vulsellum tenaculum, is inserted into the vagina and the membranes simply hooked and torn by the tip of the sharp instrument. As much fluid as possible is allowed to run away. Anesthesia is seldom necessary in multiparae, occasionally in primigravidae. In Reddoch's series of 146 cases, including 32 primigravidae, anesthesia was never found necessary. Plass employed some form of sedative (morphine or barbiturates) in about one-third of his 681 cases. It is general practice to precede the actual puncture of the membranes by castor oil and a hot enema; until recently quinine was also used routinely as a preliminary oxytocic, but the reports of Mathieu and Holman, of Reddoch, and others indicate that it does not increase the efficiency of the method. Mathieu and Holman found that their results were equally good when the castor oil, as well, was omitted, and they recommend a hot enema only as a preliminary procedure. If satisfactory pains have not ensued within four hours after rupture of the membranes, pituitrin is usually employed to accelerate the onset of labor. In Morton's practice, artificial rupture of the membranes is followed routinely at hourly intervals by nasal pituitrin until regular contractions have been established.

Contraindications.—Three conditions must be present before artificial rupture of the membranes is safe. (1) The lowermost part of the head must be at or below the level of the ischial spines. (2) The patient must be near or past her expected date of confinement. (3) The cervix must be soft and the canal less than 1 cm. long. Absence of any one of these

cases there were 11 stillbirths (1.62 per cent) and 10 neonatal deaths (1.47 per cent) with 9 of the fatalities occurring among 29 premature infants. The total fetal mortality among 652 infants weighing more than 2500 gm. was 1.8 per cent. His incidence of mild uterine infection, however, was slightly higher in this series than in his clinic as a whole.

Maternal deaths directly attributable to artificial rupture of the membranes appear to be exceedingly rare. Leo Wilson, however, reports one fatality in a patient with heart disease; after 500 c.c. of fluid had been released she became markedly cyanotic and died immediately afterward. Another patient with cardiac disease almost died after 700 c.c. of fluid escaped. The author warns against the use of the method in such patients.

In evaluating these statistics it must be recalled that they are based on carefully selected cases. With few exceptions the patients have been at or near term with the head engaged and the cervix favorable for labor. Cases of contracted pelvis and malposition have been excluded and to a considerable extent cases with the occiput posterior. In the main cases of breech presentation have also been omitted. How these figures would compare with those which might be obtained in an *equally favorable group* in which labor was allowed to start spontaneously, is not known.

INDUCTION BY BOUGIES

Except for Morton's study, published in 1930, the literature contains scant reference to the results which have been obtained by bougies in the induction of labor. In 160 cases of bougie induction, Morton found the procedure successful in 82.5 per cent of the cases; there were two maternal deaths in the series attributable to the bougies, one patient dying from uterine infection and the other from perforation of the uterus by the bougie. Among cases in which the infant was mature (2,500 gm. or more), the uncorrected fetal mortality was 9.3 per cent, the death of the child being due in six instances to prolapse of the umbilical cord. In Morton's series a single extremely large bougie (about 3 cm. in diameter) was inserted by means of a speculum, extra-ovularly, if possible.

Two small bougies (36 cm. in length, 1 cm. in diameter and fitted with wire stylet) offer certain advantages over a single large one, notably, greater ease of introduction, particularly when the cervix is closed, and less likelihood of rupturing the membranes and causing the cord to prolapse. In 50 cases of induction by means of a small bougie in the form of a catheter, Reddoch found that 18 per cent of the patients went into labor in less than two hours, 52 per cent within two to ten hours, while in 30 per cent the latent period exceeded ten hours. In one primigravida, in whom labor was induced by a catheter, labor did not ensue for three days. Two fetal deaths occurred in full-term infants and Reddoch believes these were directly attributable to the induction. He found, moreover, that intrauterine manipulation with bougie or catheter predisposed to a high maternal morbidity. Multiple small bougies have been particularly favored in England where Townsend and others have reported successful results in large series of cases. When used before the last month of pregnancy, however, the results are less satisfactory since uterine inertia and infection are not infrequent sequelae. At the Middlesex Hospital, where labor was induced prematurely in 44 primi-

not effaced; the hazard to the child, however, is definitely increased, and as the author himself states, "it should generally be used only in cases where there is an indication for the interruption."

Latent Period.—It is well known that the period from the rupture of the membranes (whether spontaneous or artificial) to the onset of definite labor is directly related to the incidence of uterine infection. Following artificial rupture of the membranes for the induction of labor, this latent period averages about three hours in primigravidae and five hours in multiparae, as reported by various authors. These average figures, however, mean very little when we are attempting to look into the hazards of the method; we are rather interested in the frequency of very prolonged latent periods since these are likely to increase the incidence of infection. Plass found that the latent period was longer than twenty-four hours in 4.7 per cent of his cases with the longest interval eighty-eight hours (almost four days). In one case, where early delivery seemed imperative, a Voorhees' bag was introduced to stimulate painful contractions. In a series of 115 cases Higgins found that contractions began within six hours in 47 per cent, within twenty-four hours in 85 per cent, but "occasionally a patient will have no pains for two days or longer." Leo Wilson, among 25 inductions by artificial rupture of the membranes, encountered one latent period of fifty-seven hours and another of forty-two hours; in the latter case rather severe sepsis followed. Among Morton's 150 cases there were two failures and one led to grave difficulties. Reddoch met one latent period of fifty-three hours among 146 cases and states that several others lasted over twenty-four hours. The longest interval found by Jackson, however, in 500 cases was only thirty hours.

It is thus clear that in the vast majority of cases the latent period following artificial rupture of the membranes is not long enough to jeopardize the safety of the patient. As we have indicated, however, almost every series reported contains one or two cases in which this interval was greatly prolonged and in which serious potentialities resulted. These occasional troublesome cases, possibly one in fifty, have no appreciable effect on average statistics so long as the patient survives, but they must not be lost sight of. They constitute, perhaps, the chief reason for believing that artificial rupture of the membranes is not always a harmless procedure but one which imposes on the patient a slight but definite risk.

Morbidity and Mortality.—When compared with clinic statistics in general the figures for maternal morbidity and fetal mortality following artificial rupture of the membranes are low. Thus, Guttmacher and Douglas found that the morbidity in their 120 cases was about one-half that usual in the clinic; their fetal mortality rate was 5.88 per cent, only a trifle higher than the rate of 5.16 per cent for the total series of the hospital. Mathieu and Holman have compared the results obtained in 750 consecutive inductions of labor by this method with their results in 750 contemporary, consecutive cases in which labor had not been induced and from which cesarean section had been omitted. The maternal morbidity was almost identical in the two groups, namely, 7.07 and 6.6 per cent, respectively, as judged by the British standard. Their gross fetal mortality in the two groups was also very similar: 4.0 and 3.8 per cent, gross, 0.8 and 1.3 per cent corrected. Among Plass' 681

Bag Induction.—Field of usefulness is limited to (1) occasional cases of premature rupture of membranes in which medicinal methods have failed to induce labor and (2) certain cases of uterine inertia.

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Béclère, C.: Undiagnosed Bilateral Hydrosalpinx, Bull. Soc. d'obst. et de gynec. 26: 381, 1937.

In 1927 Béclère first demonstrated the radiologic characteristics of clinically undiagnosed hydrosalpinx. He pointed out that this lesion is much more common than is generally believed. During the last ten years in a series of 800 hysterosalpingographies the author found more than 100 cases of undiagnosed hydrosalpinx. He has observed this condition in almost one-fourth of his sterility cases, in 15 per cent of his patients with chronic pelvic infections, in one-third of his patients with intermenstrual pain, in four-fifths of his patients with intermenstrual bleeding and in 4 per cent of women who have uterine hemorrhages of unknown origin.

Symptoms which should make one suspect hydrosalpinx are as follows: A flare-up of acute salpingitis after a mild gynecologic procedure, disappearance of masses after a flare-up, failure to relieve a chronic pelvic infection with diathermy, the presence of intermenstrual difficulties, intermittent hydorrhea and a history of pelvic peritonitis or essential ascites.

Radiological signs consist of the following: (1) The presence of spherical drops, separated from one another. This proves that lipiodol fell into a liquid. This sign is present in most cases of latent hydrosalpinx. The drops usually appear as two symmetrical masses. If they appear as a single midline mass, this is an indication of fluid in the culdesac. (2) The tubal shadow is ordinarily diffuse and irregular. If, however, it is sharp and precise a hydrosalpinx should be suspected. The author points out that the rare cases of acute salpingitis which follow hysterosalpingography in cases of hydrosalpinx are due to overdistention of the tubal cavities with lipiodol. This occurs in 5 per cent of hydrosalpinx cases.

The treatment of bilateral latent hydrosalpinx is operation or nothing at all, because treatment often leads to an attack of acute salpingitis.

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gravidæ, uterine inertia occurred in 38 per cent. The induction of labor by this method at the King's College Hospital increased the forceps rate no less than three fold, while 45 per cent of the patients showed definite evidence of uterine infection after delivery. Curling or kinking of the bougies in the lower uterine segment is not an uncommon accident when small flexible bougies are used; abnormal tetanic uterine contractions then follow without true labor pains. The position of the bougies should be checked by x-ray in questionable cases.

Bougie induction has a definite field of usefulness in cases in which artificial rupture of the membranes is contraindicated. When the cervix is long and the canal tightly closed, particularly in patients three or four weeks from term, bougie induction is preferable. It imposes a definite hazard on both mother and child, however, and should be used only on fairly urgent indication.

BAG INDUCTION

In a series of 49 bag inductions studied by Morton in 1929, he showed that the incidence of prolapse of the cord was four times greater with the bag than with the bougie, and that bag induction caused a considerably greater fetal mortality and maternal morbidity. Similar results have recently been reported by Zeisser who encountered four cases of prolapse of the cord in 35 inductions with 2 fetal deaths. There is general agreement today that induction of labor by means of the bag is the most dangerous of the several methods and has a limited field of usefulness. It is resorted to chiefly in two groups of cases: (1) Patients with premature rupture of the membranes in whom medicinal methods (nasal pituitrin, etc.) have failed to initiate labor; (2) cases of obstinate uterine inertia in which medicinal methods have failed to promote cervical dilatation.

SUMMARY

Castor Oil and Quinine.—Efficacious in 40 to 50 per cent of patients at term; harmless if dosage of quinine is 10 gr. or less.

Castor Oil, Quinine, and Pituitrin.—Efficacious in 60 or 70 per cent of patients at term; harmless if dosage of quinine is low and if administration of pituitrin (preferably nasal) is vigilantly supervised. Contraindicated in toxemias.

Artificial Rupture of Membranes.—Efficacious in 98 per cent of patients at term, provided contraindications are followed. Labor is usually shortened. In about 2 per cent of the patients the latent period is unusually long and in these cases the likelihood of infection is increased. The method is therefore not without some small danger and should be used only on definite indication, that is, when the hazard of allowing the pregnancy (presumably pathologic) to continue is greater than the slight hazard involved in the induction.

Bougie Induction.—Useful in cases in which artificial rupture of the membranes is contraindicated, particularly when patient is three or four weeks from her expected date of confinement. At that time efficacy is probably 70 or 80 per cent. Danger imposed on mother and child is greater than artificial rupture of membranes and should be used only on urgent indication.

In recent years, however, several authors have been able to demonstrate the comparative unreliability of this rule. However, too few or too incomplete observations are offered for a closer study of the condition relating to the fixation of the fetal head.

The present investigation is based on a clinical material of normal delivery cases, embracing 1,863 observations in 184 primiparas and 3,559 observations in 301 multiparas, all of whom were checked practically every day by a smaller or greater number of observations regarding the position of the fetus. Besides external, a rectal examination as a rule was also carried out.

The result of the investigation may be summed up as follows:

At examinations of normal gravidas, a movable fetal head is far more frequently found than a fixed head during the last weeks of pregnancy. This preponderance of movable heads, present in about three-fourths of the observations, is slightly smaller in primiparas than in multiparas. Even in multiparas a fixed fetal head is found during the above-mentioned period in a considerable number of examinations (about 20 per cent). In primiparas, somewhat more frequently than in multiparas, the fetal head remains constantly fixed up to the delivery.

In no less than one-third of the cases and with equal frequency in primiparas and in multiparas, alternations between fixation and movability take place as late as the last days before delivery.

Such fluctuations have been observed relatively frequently (in 45 cases) even after verification of the fixation by rectal examination. At the beginning of labor, the head (before the rupture of the membranes) is more frequently fixed in the primiparas (in two-thirds of the cases) than in the multiparas (in one-half of the cases). Approximately the same proportion is found in cases which were examined only after rupture of the membranes.

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Guthmann, H., and Bienhüls, M.: The Onset of Labor Pains, the Duration of Labor and the Time of Day, Monatschr. f. Geburtsh. u. Gynäk. 103: 337, 1936.

The authors analyzed a series of 26,707 labors and found that deliveries during the day and night were equally divided. To their own series of cases they added those of three other authors and in a total of 121,794 cases they found the incidence of day-time deliveries to be 49.1 per cent and night-time births to be 50.9 per cent. Among primiparas 48.8 per cent of the births took place at night whereas 51.2 per cent of the multiparous births took place at this time. The greatest number of births occurred at 11:00 A.M. Labor began during the night among 60.5 per cent of primiparas and among 56.9 per cent of multiparas. Since 1923 there has been a gradual decrease in the number of night-time deliveries.

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Moir, Chassar: Expulsive Force of the Uterus During Labour, Lancet 1: 414, 1936.

The author corroborates the findings of Bourne and Burn on uterine forces. In the first stage the pressure varied from 35 to 60 mm. of mercury with 45 mm. as an average. There is not much change in the magnitude of contractions during the second stage. If pituitrin is injected the tension may be increased by 90 mm. of mercury. The secondary expulsive power is important because there may be an increase of 40 or 50 mm. Even before the onset of labor, the force of the painless contractions may almost equal those during labor.

These measurements were taken by use of an intrauterine bag.

With an intrauterine tension of 15 mm. of mercury and an average increase of 45 mm. in the first and second stage is produced an average of 60 mm. pressure.

Department of Reviews and Abstracts

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Selected Abstracts

Physiology of Labor

Föderl, V.: Investigation of the Average Duration of Labor in Primiparas, Secundiparas and Multiparas and Its Relation to the Age of the Woman in Labor, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 65, 1936.

Föderl investigated the records of 10,000 women who had normal labors, normal pelves and spontaneous deliveries of babies weighing between 2,500 and 3,500 gm. born in occiput anterior rotation. The average duration of the entire labor for primiparas was fourteen hours and five minutes of which twelve and one-half hours was for the first stage, one hour and nineteen minutes for the second stage, and thirteen minutes for the third stage. In secundiparas the average duration of labor was eight hours, eight minutes, divided as follows: first stage, seven hours fifteen minutes, second stage forty-one minutes, and third stage twelve minutes. For women having 3 or more children the average length of labor was eight hours forty-one minutes, of which seven hours forty-five minutes was for the first stage, forty-three minutes for the second stage, and thirteen minutes for the third stage.

As the criterion for the onset of the first stage the author considered the onset of regular, painful uterine contractions, and as the indication for the beginning of the second stage of labor he took bearing down efforts.

Among primiparas the longest duration of labor was in the women between thirty and thirty-five years of age for in them labor lasted nineteen hours and six minutes. On the other hand, labor among women between forty and forty-five years of age was almost identical with that of women between twenty and twenty-five years old. Nevertheless, whereas in women between twenty and twenty-five years only 8 per cent required operative interference almost 70 per cent of those between forty and forty-five required assistance in labor. Hence only 30 per cent of elderly primiparas have easy labor. The explanation for this phenomenon has been offered by L. Meyer who pointed out 2 classes of elderly primiparas. The first consists of those who could not become pregnant until after many years of married life because of hypoplasia due to a primary endocrine defect. These women have difficult labors. The second group consists of elderly women who did not conceive earlier for economic, social or other reasons. These women give birth to children as easily as young individuals.

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Marcus, H.: Fixation of the Fetal Head During Pregnancy, *Acta obst. et gynec. Scandinav.* 16: 356, 1936.

The classical rule that the fetal head during the latter part of pregnancy is fixed in the pelvis in a primipara, whereas in a multipara it remains movable up to delivery, is generally emphasized in the textbooks.

v. Numers, C.: *A New Method of Diagnosing Rupture of the Membranes*, Acta Obst. et gynec. Scandinav. 16: 249, 1936.

For the purpose of diagnosing rupture of the membranes in the course of labor, the writer attempted, by means of Sudan staining, to prove the occurrence in the vaginal secretion of free drops of fat or expelled cells of the fetal sebaceous glands derived from vernix caseosa. Through a glass speculum one drop of secretion is taken with a platinum loop and spread out on a carefully defatted slide. The preparation is air-dried and stained at room temperature in a dye solution, 0.2 to 0.3 gm. Sudan III in 100 c.c. of 70 per cent hot alcohol. The slide is washed in water, dried and examined immediately under low magnifying power. The fat substances are stained a distinct orange red; particles of mucus are sometimes stained weakly yellowish red. Of 141 samples taken before rupture of the membranes only 4 gave a slight positive Sudan reaction, the rest yielding a negative result (97.2 per cent). Of the 139 samples taken after rupture only one gave a negative reaction. Slight Sudan reactions seem to be relatively more frequent in premature cases. The faulty reactions amount to about 2 per cent of the entire material.

J. P. GREENHILL.

Endres, P.: *Does Premature or Early Rupture of the Membranes Influence the Length of Labor*, Monatschr. f. Geburtsh. u. Gynäk. 105: 216, 1937.

Contrary to the general belief, Endres found that premature rupture of the membranes before the onset of labor shortened labor. This was true even when pregnancy was terminated prematurely or postmaturely. The shortening of labor takes place during the first stage. Hence the absence of the bag of waters not only does not influence the period of dilatation unfavorably, but it actually helps dilatation in many cases. The reason for this, in the opinion of the author, is the absence of resistance which is present when hydrostatic pressure is exerted by an intact bag of waters.

On the other hand, rupture of the membranes after the onset of labor pains but before complete dilatation of the cervix, prolonged labor. In these cases the increase in labor is due to a prolonged first stage. The cause for this is a temporary atony of the uterus which follows rupture of the membranes.

The practical significance of these findings is that premature rupture of the membranes is a justifiable procedure in certain cases. Above all, when premature rupture occurs spontaneously, drugs should not be given to hasten labor pains because they may have a detrimental effect.

J. P. GREENHILL.

Reiles: *Induction of Labor in Cases of Premature Rupture of the Membranes*, Bull. Soc. d'obst. et de gynec. 25: 337, 1936.

Reiles employs the Stein method of inducing labor. In a series of 76 cases labor was successfully induced in 64, i.e., in 84.2 per cent. In all the cases where labor was not induced the cervix was long and uneffaced. The average duration of labor in the successful cases with spontaneous deliveries was eight hours and forty-eight minutes for the primiparas and four hours for the multiparas. No harm to the baby was observed.

J. P. GREENHILL.

Sunde, A.: *Spontaneous and Artificial Rupture of the Membranes During Labor*, Acta obst. et gynec. Scandinav. 17: 133, 1937.

In 9,375 full-term labor cases observed at the Oslo Woman's Clinic, the time of rupture of the bag of waters was known. The author found that rupture of

With these pressures and an additional 45 mm. from secondary expulsive forces, a total average of 105 mm. of mercury pressure is transmitted to the fetus during parturition.

II. CLOSE HESSELTINE.

Léon, J., and Ferrari, R. A.: Our Abdominal Belt for the Second Stage of Labor, *Bull. Soc. d'obst. et de gynéc.* 25: 417, 1936.

The authors are of the opinion that their abdominal belt decreases the duration of labor not only among multiparas but among primiparas as well. It does this without increase in the frequency of perineal lacerations. The use of this belt reduces the necessity for the use of pituitrin during the second stage of labor. It also reduces the frequency of Kristeller expression and the use of forceps. In the extraction of babies by the breech the belt prevents deflection of the head and dislocation of the arms. After symphysiotomy the belt permits spontaneous delivery without the use of oxytocics.

J. P. GREENHILL.

Ehrhardt, K., and Henss, E.: The Artificial Induction of Labor in Postmature Pregnancy, *Med. Klin.* 32: 1700, 1936.

The authors used castor oil, quinine, and pituitary extract to induce labor in 322 cases of overterm pregnancy and were successful in 80 per cent. Multiparas reacted more favorably than primiparas. In the primiparas where labor was successfully induced, the duration of the labor was shorter than normal. The best results were obtained in women who had gone one or two weeks past term. There was no apparent increase of forceps deliveries or uterine atony after artificial induction of labor. The authors point out that by these means it is easy to bring about expulsion of a dead baby or a hydatidiform mole.

J. P. GREENHILL.

Reiles, M.: Artificial Induction of Labor, *Rev. franç. de gynéc. et d'obst.* 31: 335, 1936.

The author employed the Stein method in 86 cases. The chief indication was premature rupture of the membranes which occurred in 77 cases. The method proved successful in 71 cases or 82.5 per cent. In four of these cases two and in 3 cases three attempts were made before success was accomplished. In 62 of the 71 successful cases, delivery was spontaneous. The average duration of labor after induction was eight hours and forty-eight minutes for primiparas and four hours for multiparas. No child was lost because of the induction of labor. The total morbidity for the series was 18.6 per cent.

J. P. GREENHILL.

Movers, F.: Medical Induction of Labor, *Monatschr. f. Geburtsh. u. Gynäk.* 104: 184, 1937.

Labor was induced medically in 213 women who were at or beyond term. In 40.7 per cent of the cases labor was terminated within twenty-four hours. However, if the cases of repeated induction are excluded, the incidence of success was only 35.1 per cent. The combination of quinine with pituitary extract was more successful than quinine, calcium, and pituitary extract. However, quinine and calcium gave better results than quinine alone. Among the successful cases, labor was terminated by operative means in 19.6 per cent. The author's method of inducing labor is a modification of Stein's procedure.

J. P. GREENHILL.

than ordinary medical induction of labor. The author advises the use of a rectal bag only as an aid in the induction of labor at term in cases of premature rupture of the membranes.

J. P. GREENHILL.

Purandare, N. A.: Anterior Shoulder as a Guide to the Engagement of the Head and the Progress of Labour, *J. Indian M. A.* 5: 457, 1936.

The author points out that the greater the skill of abdominal examinations for recognizing different positions of the fetus in utero, the fewer vaginal examinations there need be with their attendant risk of introducing infection.

The anterior shoulder serves as a valuable guide to the progress of labor. It is easily palpable; it can be readily marked on the abdominal wall; its descent can be followed, and as it approaches the midline and crosses it and goes over to the other side, it indicates, especially in occipitoposterior positions that internal rotation of the head is taking place. The height of the anterior shoulder from the top of the symphysis pubis can be measured and from it the relation of the head to the pelvis judged. These heights are especially useful in cases being given a test of labor. When the head is above the pelvic brim the shoulder is $4\frac{1}{2}$ to 5 inches above the symphysis; when in the brim 4 inches; in the mid-cavity 3 inches; when at the outlet 2 inches; when at the pelvic floor $1\frac{1}{2}$ inches. These estimates were obtained from several hundred cases.

In occipitoposterior positions the anterior shoulder gives valuable information during labor. When the shoulder approaches the midline, it is a favorable indication of a spontaneous outcome of labor. When, however, even after rupture of the membranes the shoulder remains in the pararectal line, it indicates that internal rotation of the head has not begun.

F. L. ADAIR AND S. A. PEARL.

Levy-Solal, E., and Sureau, M.: Concerning the Period Known as "Physiologic Rest" During Normal Delivery, *Bull. Soc. d'obst. et de gynec.* 25: 221, 1936.

The authors believe that the so-called "physiologic rest" of labor pains after delivery is purely a theoretic conception. After the expulsion of the fetus there is usually a period during which the uterus is retracted and does not evidence any contractions. However, the studies of the authors have shown that the uterine contractions commence within a few minutes after the expulsion of the baby. These contractions increase in duration and intensity and produce the pain which the patient feels during the early puerperium. The cessation of contractions immediately after delivery constitutes an anomaly which prevents separation of the placenta. Hence, in the opinion of the authors, actual rest of the uterine muscle after the baby is born is not a physiologic but a pathologic condition. Anesthetics usually increase this period of rest and occasionally produce bleeding from the uterus. On the contrary, oxytocics increase the uterine contractions and hasten separation of the placenta.

J. P. GREENHILL.

Miller, Douglas: Common Obstetrical Injuries and Their Sequelae, *Brit. M. J.* 2: 4, 1936.

The author discusses injury to the pelvic floor, to the anterior vaginal wall by overstretching, to the lateral cervical ligaments caused by the application of forceps before the cervix is fully dilated; laceration of the cervix, especially in

the membranes before the onset of labor occurred in 13 per cent of the cases. It was more frequent in primiparas than in multiparas, and in older women. The risk of infection was greater after primary rupture than in the cases where the membranes ruptured after labor pains had started. The earlier the rupture the greater was the risk of infection.

J. P. GREENHILL.

Wichmann, S. E.: Rupture of the Membranes During Labor, *Acta obst. et gynec. Scandinav.* 17: 158, 1937.

Wichmann studied large series of primiparas and secundiparas and found that premature escape of fluid occurred with equal frequency in primiparas and multiparas and in about 10 or 12 per cent of women between twenty and twenty-four years of age. The tendency increased somewhat with age. The shortened period of labor usually observed in these cases is due to the nonpainful contractions which had occurred during the latent period. There was no increase in operative delivery, morbidity, mortality or prolapse of the cord in the cases of premature rupture of the membranes. Labor seems to be shortened by artificial rupture of the membranes but routine rupture of the bag of waters to hasten labor should be condemned.

J. P. GREENHILL.

Essen-Möller, E.: Has Premature Rupture of the Membranes Any Influence on the Progress of Labor, *Acta obst. et gynec. Scandinav.* 16: 1, 1936.

The author studied 1,000 cases of premature rupture of the membranes, and also 300 cases in which the membranes were ruptured artificially. He found that premature rupture of the membranes occurred much more frequently in multiparas than in primiparas. In the cases where the membranes ruptured prematurely, labor both in the primiparas and in multiparas was shorter than in women with intact membranes. Infection did not occur more often in premature rupture than in ordinary labor. Where infection did arise it occurred much more frequently after operative interference than after spontaneous labor. Operations were performed much more frequently after premature rupture of the membranes than otherwise. However, this did not result in an increase of either maternal or fetal mortality. Prolapse of the cord did not occur more frequently after premature rupture of the membranes.

When artificial rupture of the membranes was performed, more infections resulted than after spontaneous rupture of the membranes. Likewise operative interference had to be resorted to more frequently. Both the maternal and fetal mortality were higher after artificial rupture of the membranes than after ordinary labors or after spontaneous rupture of the membranes. The author concludes that the old apprehension concerning the danger of premature rupture of the membranes is not founded on facts. However, when the membranes are ruptured artificially, serious complications may result for both mother and child occasionally. Hence, the author warns that the membranes should not be ruptured artificially except for definite indications. He condemns the routine rupture of the membranes simply to hasten or shorten labor.

J. P. GREENHILL.

Günther, W.: Procteurysis (Rectal Tokokinesis) and Its Value as an Aid to Medical Oxytocics, *Monatschr. f. Geburtsh. u. Gynäk.* 106: 138, 1937.

Procteurysis was employed in a series of 360 cases where the membranes had ruptured. Günther found that the best results were obtained when this procedure was combined with the use of quinine. He also found that procteurysis was no better

Peck, H. A.: *Analgesia in Labor*, N. Y. State J. M. 36: 705, 1936.

Peck records his experience with the Gwathmey method in a consecutive series of 400 personally conducted cases.

The degree of the patient's discomfort rather than the degree of dilatation is preferred as an index of the analgesia necessary. The advantages of the method are: safety, availability for home or hospital use, practical lack of contraindications, economy, and ease of application. The comparative rarity of maternal and fetal complications is stressed. Low forceps and episiotomies of election were done in a considerable percentage of cases as a conservative measure.

There were no fetal deaths attributable to the method.

J. P. GREENHILL.

Prys-Jones, T. B.: *Painless Labour*, Brit. M. J. 2: 627, 1936.

At a time when the dangers and perils of childbirth are being somewhat widely and unduly aired in the popular press, the author finds it opportune to report a case of completely painless labor in an eighteen-year-old primipara, a domestic servant. The child was born within a period of ten minutes with a complete absence of labor pains, while the mother was at stool. The mother showed no evidence of fatigue or shock. The blood loss was normal, although the placenta remained in the vagina some two hours. The infant, 7 pounds, survived despite its rescue from a primitive earth closet.

F. L. ADAIR AND S. A. PEARL.

Items

NATIONAL COMMITTEE ON MATERNAL HEALTH

AN IMPORTANT NEW PROGRAM FOR RESEARCH

THE National Committee on Maternal Health, with headquarters in New York City, is engaged in formulating and effecting a program for the study of medical and social factors of human reproduction.

The necessity for a reconsideration of the former aims and work of the Committee was recognized last fall. It had gradually become clear that the publication program had been practically completed. In other words, most of the available knowledge in the Committee's field of activity had been compiled and given to the interested public in the form of books on various aspects of the field of maternal health. Various specific research projects were already under way. Future progress appeared to lie, then, in investigation rather than in compilation, since for the moment endeavors in the latter direction seemed to have reached a natural conclusion.

The field for further research in subjects occupying the borderland between the medical sciences on one side and the social sciences on the other, remained wide open for further study. No other organization has entered this region intensively. The biologist has advanced far into the field of infrahuman sexual physiology, but he has stopped short at the boundary of human problems. The physician has limited himself to

primiparas; injury to the rectal fascia with its subsequent herniation and production of a rectocele; complete perineal tears, most often incurred in delivery of a breech in a primipara, or in the delivery of a face presentation. The avoidance of difficult labor by antenatal recognition of disproportion; careful determination of the position of the head before forceps are applied; conservatism in the use of forceps unless and until the head is low in the pelvis, and the avoidance of unnecessary overstretching of the vaginal walls and subjacent tissues by unduly withholding assistance; the evacuation of the bladder at regular intervals during labor and especially before forceps are applied; these are elementary obstetric principles, the observance of which may prevent much of the invalidism that follows childbirth.

The simple operation of episiotomy is a special prophylactic procedure and highly recommended. The care and skill with which injuries are repaired bears directly upon the prevention of subsequent disability. The practice of discharging patients on the eighth or ninth day after confinement is greatly to be deplored. Rest, massage and exercise are useful to restore tone in overstretched muscles. A well-fitting corset and a pessary may be valuable adjuncts postpartum. The smallest size pessary that is effective should be used so as to interfere as little as possible with involution of the vagina, and it should be replaced at frequent intervals by smaller sizes until involution is complete.

The development of genital prolapse is by no means always preventable, however.

F. L. ADAIR AND S. A. PEARL.

Barr, Adam, and Tindal, Andrew: A New Machine for the Self-Administration of Gas-and-Oxygen Analgesia in Labour, *Lancet* 1: 1271, 1937.

An apparatus for administering nitrous oxide and oxygen gas has been developed, intended for self-use by the patient in the late first and second stage. It is claimed to be safe, to deliver only a fixed proportion of gases, and to be economical, easily portable, and easily manipulated, yet efficient.

One hundred consecutive cases treated with this apparatus are reported, and in only 8 did it prove unsatisfactory. Chloroform was used in 6 patients who had forceps deliveries. There were no stillbirths or neonatal deaths. Cyanosis was not observed.

H. CLOSE HESSELTINE.

Banssillion, E., and Bucher, P.: Local Anesthesia of the Perineum During Obstetrical Interventions, *Rev. franç. d. gynéc. et d'obst.* 31: 858, 1936.

The authors make a plea for the more extended use of local infiltration of the perineum during labor either alone or combined with a general anesthetic. This procedure may avoid the necessity for an episiotomy. The authors report a series of 13 cases in which they employed infiltration anesthesia successfully.

J. P. GREENHILL.

Petersen, E.: Obstetrical Sodium Evipan Anesthesia, *Acta obst et gynec. Scandinav.* 16: 261, 1936.

Petersen analyzed the results obtained in 100 women who had been given sodium evipal as an anesthetic. In all the cases a satisfactory anesthesia was obtained. The author believes this form of anesthesia is superior to chloroform. No harmful effects were observed on mother or fetus.

J. P. GREENHILL.

3. *Abortion*, in particular certain aspects of its prevention; the social causes back of induced abortion, with especial attention to recidivism; the subsequent fertility of frequently aborted women; and the impact of abortion on the family. Abortion is an almost untouched problem in the social field, and yet it is responsible for an important part of America's notoriously high maternal mortality rate.

4. *Sterilization*, in particular the development of a practical standardization of medical and eugenic indications for the use of the general physician or surgeon.

5. *Marriage consultation*, to be studied in a medically controlled center set up so that a better understanding of the problems of married life can be obtained, and the efficacy of certain forms of advice or therapy can be scientifically measured, as in other medical studies.

The New York charter of the National Committee on Maternal Health is elastic enough to make proper any of the studies envisaged in the new program. However, certain modifications of organization and operation may be made in order to render the Committee's work effective.

HOWARD C. TAYLOR, JR., *Secretary*.

The American Congress on Obstetrics and Gynecology

Preparations for holding The American Congress on Obstetrics and Gynecology are proceeding, several meetings having been held by the members and directors of The American Committee on Maternal Welfare, Inc., to develop the arrangements for convening the Congress in Cleveland during the week of September 11, 1939. Cleveland was selected as offering an easily reached central point with adequate hotel facilities and suitable meeting and exhibition space in the Convention Hall.

The Congress has been organized to include the interests of various groups of participants, such as medical educators, physicians, nurses, public health workers, hospital administrators, and others interested in the problems of human reproduction. The morning sessions are allotted for the presentation of scientific and technical papers in each group; in the afternoons mixed groups will participate in general discussions, and the evening sessions will be for the public, probably with broadcasts.

In addition there will be commercial and scientific exhibits developed to illustrate the work of various public and private agencies, and of individuals engaged in scientific activities pertaining to human reproduction. Those exhibits of a commercial character, as of instruments, books, apparatus, medicinal preparations, etc., will be of a high character and ethical in presentation.

An executive office devoted to the management of the Congress has been opened at The Annex of The American College of Surgeons, 650 Rush Street, Chicago, in charge of the General Chairman, where all inquiries may be addressed.

The directors of The American Committee of Maternal Welfare, Inc., are the governing body for the Congress, and are as follows: the Drs. George W. Kosmak, LeRoy A. Calkins, Robert L. DeNormandie, Robert

the more or less traditional concept and treatment of disease, including infection, trauma, new growths, and definitely abnormal psychologic conditions; but through the natural limitations of his time and technique, he has given up the trail when it appeared to lead him into unfamiliar sociologic or biologic fields. The sociologist, who until the present time has rarely shown much clinical instinct, has terminated his studies where the problem approached the field of medicine. Furthermore, most previous studies of sex biology have applied to a single sex. Yet the major portion of the population are aware of sex response or traumata in relation to the other sex. It seems important, then, in these border-line fields to study phenomena of sex biology in relation to the partner, particularly in the married couple. Accordingly, there appears to be a large area for study lying between medical and biologic fields on the one hand and social fields on the other, for which no research group is at present taking particular responsibility. This accounts for the new program of the National Committee on Maternal Health.

The Committee desires to establish itself as an impartial student of the medical, social, and psychologic factors of human reproduction. It has recognized the possibility of being influenced by either one of two types of thought: the sentimentality which in America attaches to a liberal or a radical point of view; or the determined conservatism which is active and effective in this field, especially as exemplified by organized medical bodies.

It is the strong feeling within the Committee that its work should be an unbiased and objective examination of the facts with commitment to no interested parties. This orientation is in accord with the new criticism with which many of the aspects of sex study and reform are being considered. Such a policy may involve the re-examination of many of our previously accepted tenets, but it is only by such a policy that the National Committee on Maternal Health believes it can exercise the influence that will give its work importance.

The Committee would endeavor to act in two capacities:

1. As a council to coordinate and advise research in its special field.
2. As an organization for actual research in problems of human reproduction, essentially those dealing with aspects of conception, by members or under the direction of members of the Committee. To this extent the Board of Directors has been enlarged to include representatives of pertinent disciplines and techniques: gynecology, obstetrics, urology, psychiatry, biology, and experts in the study of the family.

In both of these capacities the study of problems outlined in a carefully worked out plan is to be stressed, in which the techniques of the specialties just enumerated will focus on the problems under attack. This program includes five main heads:

1. *Sterility*, with special emphasis on psychologic and eugenic aspects, as well as on attempts toward therapy. The former are not covered by the conventional routine clinical study, and constitute problems of steadily increasing importance.
2. *Contraception*, including especially (a) a testing of methods; (b) a consideration of the physical, mental, and social effects within the family situation; and (c) possibly an attempt to work out a regulation of contraceptive practice in the face of our falling birth rate and in the interests of good public health and social well-being.

Second All India Obstetric and Gynaecologic Congress

The Congress will be held at Bombay from April 13 to 16, 1938. A medical exhibition is also arranged as part of the program. Subjects selected for official discussions are: Toxemia of Pregnancy and Carcinoma of Cervix.

The Congress will be inaugurated by the Prime Minister, the Government of Bombay and the medical exhibition will be declared open by the Minister of Health. Dr. B. D. Mukherji of the Carmichael College, Calcutta, has consented to preside. All obstetricians and gynecologists are requested to attend the Congress.

Further information can be obtained from the organizing secretary, Raj Bhuvan, Sandhurst Road, Bombay 4.

Books Received

MANUAL OF OBSTETRICS. By Thomas Watts Eden, Past President of Royal Society of Medicine, etc., and Eardley Holland, Obstetric and Gynaecological Surgeon, and Lecturer on Obstetrics and Gynaecology, London Hospital, etc. Eighth edition, 765 pages, with 12 plates and 398 illustrations in the text. J. & A. Churchill, Ltd. London, 1937.

SYNOPSIS OF OBSTETRICS AND GYNAECOLOGY. By Aleck W. Bourne, Consulting Obstetric Surgeon, Queen Charlotte's Hospital, London, etc. Seventh edition, fully revised, with numerous diagrams, 452 pages. William Wood and Company, Baltimore, 1937.

VITAMINHAUSHALT IN DER SCHWANGERSCHAFT. Mit besonderer Berücksichtigung der Vitamine A und C. Von Dr. med. Gerhard Gachtgens, Universitätsfrauenklinik zu Leipzig. Mit 21 Abbildungen, 161 Seiten. Verlag von Theodor Steinkopff, Dresden, 1937.

WUNDVERSORGUNG UND WUNDBEHANDLUNG. Von Professor Dr. H. v. Seemen, chirurgische Universitäts—Klinik Muenchen. 66 Seiten. Verlag von Ferdinand Enke, Stuttgart, 1938.

D. Mussey, Everett D. Plass, and Philip F. Williams. The general chairman is Dr. Fred L. Adair. Dr. Rudolph W. Holmes is Treasurer of the Congress and Dr. James R. McCord is Secretary. The organization of the committees is not yet completed but the following chairmen have been selected: Budget and Finance, Dr. Walter T. Danureuther; Program, Dr. Frederick H. Falls; Arrangements, Dr. Joseph L. Baer; Membership, Dr. Philip F. Williams; with Dr. Buford G. Hamilton as Secretary.

The other committee chairmen and the personnel of the committees' subcommittees representing various interested groups, will be selected as rapidly as possible.

The executive secretary has not as yet been appointed. The officers of the Congress are desirous of enlisting the cooperation of all interested groups and individuals, and are glad to receive inquiries and suggestions from various sources.

The work of the Congress is being handled by several committees, and further announcements of these will appear in subsequent issues of medical, nursing, and other journals.

American Board of Obstetrics and Gynecology

The oral, clinical, and pathological examinations for Group A and Group B applicants will be held in San Francisco, California, on Monday and Tuesday, June 13 and 14, 1938.

An informal dinner for the Diplomates of this Board, their wives and others interested in the work of the Board, will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, will address the group, and the successful candidates of the preceding two days' examinations will be introduced in person. Tickets, at \$2.25 each, may be obtained in advance from Dr. Joseph L. Baer, 104 S. Michigan Avenue, Chicago, Illinois, or at the door. Reservations should be made in advance if possible.

Application for admission to the June, 1938, Group A examinations must be on file in the Secretary's office before April 1, 1938.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

British Congress of Obstetrics and Gynaecology

The Eleventh British Congress of Obstetrics and Gynaecology will be held in Edinburgh on April 4, 5, and 6, 1939, under the presidency of Prof. R. W. Johnstone, C.B.E. For further information, please communicate with the senior local secretary, Dr. E. Chalmers Fahmy, 7 Chester Street, Edinburgh, 3.

hormone would be of value. Thus far the tests reveal the blood level of the hormone to be at its peak in the last part of the cycle while the level of the hormone in the urine is highest in the middle of the cycle. Obviously these findings tend to confuse the problem. From experiments on the motility of the human uterine musculature in the presence of the corpus luteum hormone and its reaction to pituitrin, on the various days of the cycle, Knaus (1929) concluded that physiologic ovulation occurred fifteen days before the ensuing period in women with normal reproductive physiology. Unfortunately, his results are not substantiated by most of the other investigators.

According to Papanicolaou (1933), studies on the changes in the vaginal epithelium reveal that in one-third of women near the time of ovulation vaginal smears show large and characteristic cells with a marked decrease or absence of leucocytes and often an increase in the amount of mucus. At the time of ovulation there is a decrease in the mucus with an increase in the number of leucocytes and a scaly type of cell, sometimes accompanied with red blood cells. From these observations Papanicolaou believes that ovulation occurs frequently on the twelfth and thirteenth days.

As a result of his examination of the endometrium in 898 cases, Schroeder (1928) concluded that ovulation occurred upon the fourteenth to sixteenth day of the cycle. This study, based upon microscopic examination of the endometrium which was correlated with the menstrual data of patients who had a twenty-eight-day cycle, has been questioned by some; for in the first place the patients' memories may have been unreliable and second, the entire endometrium was not always available for study.

TABLE I. NUMBER OF DAYS INTERVENING BETWEEN MENSES

SUBJECT	OWN ESTIMATE OF INTERVAL DAYS	ACTUAL INTERVAL				
		1	2	3	4	5
1	21-24	26	24	24	27	—
2	28-34	28	24	27	31	32
3	28	29	25	28	28	—
4	28	30	27	28	28	—
5	38-46	50	33	31	—	—
6	26	26	24	26	22	25
7	30	32	35	32	30	—
8	28	30	35	29	31	—
9	28	26	30	28	28	27
10	28-30	Pregnant				
11	23-27	30	22	—	—	—
12	28-32	29	31	25	27	—

A similar objection is raised to the simple biopsy method, since sections taken in the same patient from different areas of the endometrium often present variable histologic pictures. Observations based upon instances of isolated coitus followed by pregnancy and cases of success-

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Original Communications

BIO-ELECTRIC CORRELATES OF THE MENSTRUAL CYCLE IN WOMEN*

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*(From the Departments of Neuro-Anatomy and Obstetrics and Gynecology,
Yale School of Medicine)*

THE PROBLEM

RECENTLY there have appeared two reviews of the literature dealing with the time of ovulation in women (Knaus 1929, Hartman 1936). From these it is evident that a wide variety of techniques have been used in the analysis of this problem. The methods employed have ranged all the way from a determination of the time of the greatest sex desire to the observation of the ovaries at laparotomy. Inasmuch as direct studies of the human female have given suggestive but not conclusive evidence, numerous observers have sought the answer in studies of ovulation in infrahuman mammals.

Of the various lines of approach, much has been made of the examination of the corpus luteum at the time of operation. The majority of gynecologists present evidence to show that records of the age of the corpus luteum indicate that ovulation occurs between the fourteenth and sixteenth days of the menstrual cycle. Novak (1934) and others are of the opinion that it is impossible to correctly estimate the age of the mature corpus luteum even from histologic examination.

Since the development of the corpus luteum is believed to be due primarily to the hormone activity of the anterior lobe of the pituitary gland, it might be assumed that tests of the blood and urine for this

*Aided by a grant from the Josiah Macy, Jr. Foundation.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

THE TECHNIQUE

The procedure employed was exactly like that described by us (1936). As nearly as possible, daily determinations were made on each individual with the exception of Sundays, holidays, and vacations. The index finger of each hand was placed in a beaker of physiologic salt solution which was in direct contact with the salt solution of the electrode chambers through glass tubing. Five successive determinations were made at each sitting, the fingers being removed from the salt solution between each reading. The values obtained were averaged for each day, and graphs prepared for each individual. Results strikingly similar to those previously reported were found with certain highly interesting differences. Attention should be called to the fact that there is no direct explanation of the mechanism involved in the production of changing bio-electric potentials which seem to correlate with the menstrual cycle. Nevertheless, it must be borne in mind that the technique used was developed in order to study more rigorously the possible presence of an electro-dynamic field in all living systems (Burr 1932; Burr and Northrop 1935; and Northrop and Burr 1937). A considerable number of studies attest the presence of such a field, and it seems not unlikely that some of the properties of this field of the organism correlate with such fundamental physiologic processes as the menstrual cycle.

RESULTS

Consideration of the data reveals that the determinations are made at the index fingers, a considerable distance from the major physiologic activities associated with menstruation. The correlations which have been noted are astonishing, and no ready explanation is at hand for the obvious "action at a distance." However, two possibilities may be considered. The presence of negative currents of injury has long been noted by physiologists, and since the menstrual flow is associated with the breakdown of tissue it might, therefore, be expected to show such currents. Yet the data demonstrate that the period of the menses is a period of low voltage difference between the two index fingers. Moreover, the peaks of potential difference to be seen in the intermenstrual period seem unrelated to any extensive injury of the genital tract, although it cannot be denied that the rupture of the egg from the follicle is associated with a minimum amount of injury.

However, the ovulation studies of Burr, Hill and Allen (1935) show that the voltage rise between the symphysis and the vagina in the rabbit develops parallel with the increase in size of the follicles, with a rapid return to the base line after the egg leaves the follicle. It is difficult to see, therefore, how negative currents of injury could explain the phenomena, nor does any immediate explanation arise from the fact that the activity in the pelvis is reflected in the finger tips. If, however, it

ful artificial insemination suggest that ovulation occurs most frequently at the middle of the menstrual cycle.

Newell, Allen, Pratt and Bland (1930) recovered five unfertilized human ova from the Fallopian tubes at operation, and concluded that ovulation in these instances had occurred a day or two before the fourteenth day of the cycle. Attempts to deduce the time of ovulation from a study of embryos and the dates of menstruation are thus far of little value and, because of the lack of accurate information, unsatisfactory. It is clear that the weight of evidence suggests that ovulation in women occurs during the middle of the menstrual period, and similar investigations in monkeys seem to confirm this.

From a study of ova recovered at laparotomy, Corner and Allen (1929) concluded that ovulation took place between the eleventh and fourteenth days of the cycle. By rectal palpation, Hartman decided that ovulation takes place in the monkey on the average between the twelfth and thirteenth days, while the range is from nine to eighteen days. By the vaginal smear method, Davis and Hartman (1935) found that while the exact time of ovulation could not be determined, it never occurred in the late premenstruum but usually about the middle of the cycle. In analyzing 52 pregnancies which resulted following 420 copulations on various days of the cycle in monkeys, Hartman (1936) found that 49 occurred from coitus on the eleventh to the sixteenth days inclusive of the menstrual cycle.

Inasmuch as Burr, Hill and Allen (1935) were able to show marked rises in potential difference associated with ovulation in the rabbit, it was suggested that the rise in potential difference in the human female might also be associated with ovulation.

Recently we (1936) observed marked variations in the bio-electric potential difference between the index fingers of the two hands in the human female which correlated with the evidence of the menstrual cycle. They reported that normally the right index finger was several hundreds of microvolts positive with respect to the left. During the menstrual flow, however, this voltage difference decreased significantly and on occasions showed a positive potential in the left index finger. In addition, between the fourteenth and seventeenth days preceding the onset of the subsequent menses, the right index finger showed an increase in positive polarity amounting to several thousands of microvolts. For nine successive months, the electrical cycle repeated itself with astonishing accuracy. Similar records from a pregnant female showed an entire absence of such monthly cyclic phenomena. In order to extend these observations on a larger scale, finger to finger tests were made on fourteen women for three successive months. Of these, one was in the period of normal menopause, one artificial menopause following a panhysterectomy with bilateral salpingo-oophorectomy, 8 were single, 3 married, and 1 married and pregnant.

there was a ringworm infection treated by x-ray. In the case of the panhysterectomy, there are two elevations of voltage difference for which no correlate could be determined.

In Fig. 2 are to be seen graphs of those individuals in which a marked rise in the potential differences was found in and around the middle of the menstrual period. In Patient 1, in four months, only one genuine peak was recorded but it will be noted that this patient was absent on corresponding days of each of the three other cycles. Patient 2 was difficult to classify in that during the second and third

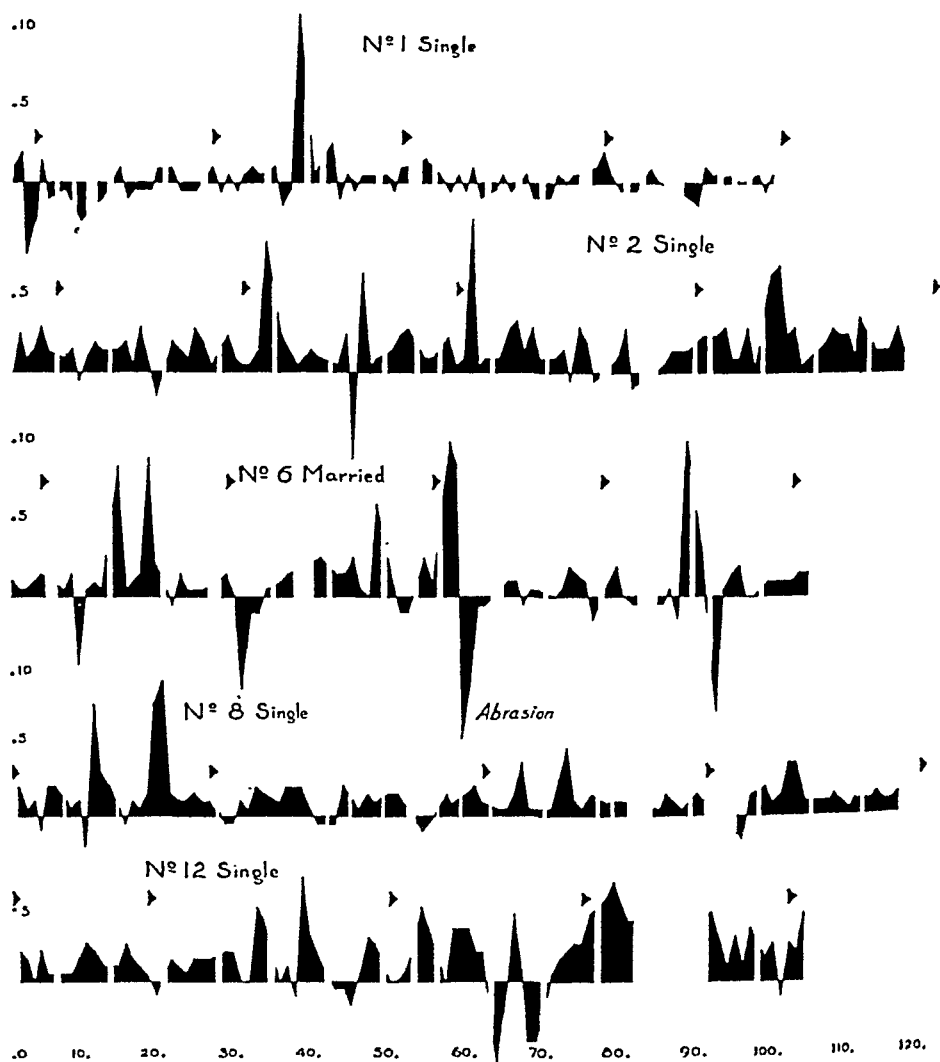


Fig. 2.—Similar graphs from individuals showing marked rises in potential in and around the middle of the period.

months peaks occurred right after the menses; whereas in the fourth month it occurred about the middle of the period. In Patient 6 peaks occurred in the middle of the cycle during the first and the last month but during the third period a peak showed immediately following menstruation. Patient 8 showed two high peaks in the first period, none in the second and no peaks in the third and fourth periods. Patient 12 was difficult to classify since there seemed to be little regularity.

In Fig. 3 are graphs from patients showing the greatest electrical differences in the few days immediately following menstruation. Patient 7 showed the greatest irregularity of any of those studied. A peak was observed at the end of the first

is assumed that the living organism possesses an electrodynamic field, such profound physiologic rhythms as are associated with the menstrual cycle might be expected so to modify the entire field that evidences of local activity could be detected anywhere throughout that field. At present no experimentally demonstrated set of facts is available to explain the origin and propagation of these bio-electric potentials. A great deal of careful analytical work will be required before this question can be answered. The data collected are presented in graphic form in Figs.

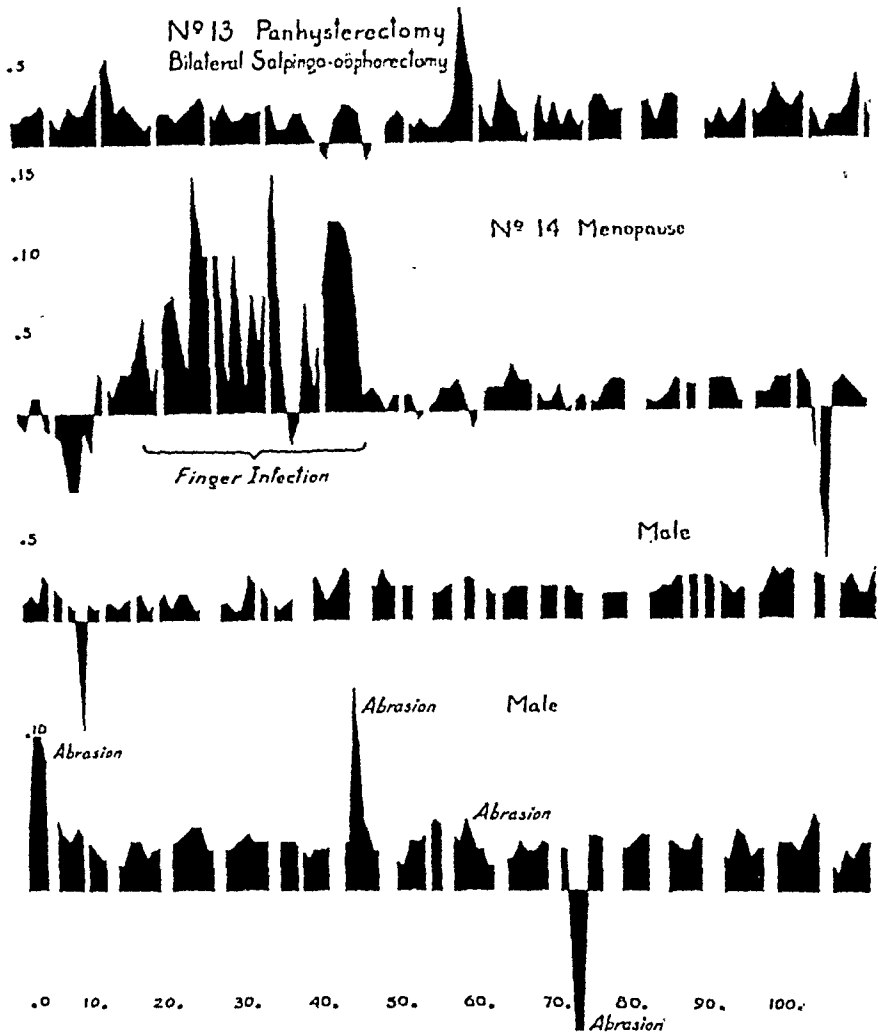


Fig. 1.—Plots of voltage difference in two males and two females in millivolts against successive days. Note effect of extraneous factors such as abrasions and skin infections.

1 to 4. It will be seen at once that this pattern is a highly variable one, not always consistent with the same individual.

The four graphs in Fig. 1 are from two males and two females. One of the females was in the menopause and the other had a panhysterectomy. The two males showed no cyclic phenomena whatever and in the second instance in particular, the only marked voltage differences detected were those which were associated with minor abrasions, cuts, or hangnails on the fingers being tested. A similar irregularity is to be seen in the individual with the normal menopause in whose left index finger

Fig. 4 shows the two patients with marked differences from any of the others. Patient 11 would seem to be completely anovulatory if the rise in voltage difference observed is to be correlated with ovulation. In any event, no significant voltage shifts were observed. Patient 10 is particularly interesting because of pregnancy. A comparison of this curve with that derived from another pregnancy (Burr and Musselman, 1936, Fig. 2) shows an astonishing similarity. The three deviations from the baseline in both patients occurred at approximately the same time in pregnancy and the voltage shifts were in the same direction. Correlates for these deviations are entirely unknown.

The above data can be examined from a somewhat different angle. In the group under observation, Patients 1, 2, 4, 7, 8, 9, 11, and 12 were single. Patients 3, 5, and 6 were married and Patient 10 was married and pregnant. The graphs of the married women, Numbers 3 and 6, show signs of greater bio-electric activity than was to be seen in any of the single women except Patient 7. If it should turn out that these peaks are genuinely associated with ovulation, these data suggest a possible correlation between coitus and ovulation.

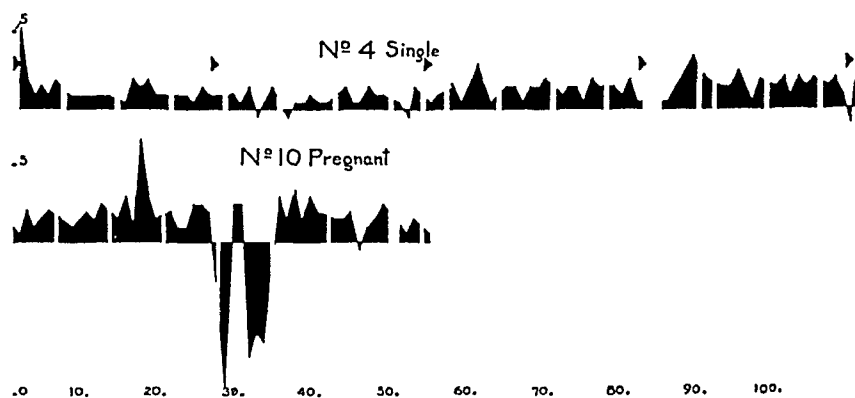


Fig. 4.—Two graphs, one from an apparently anovulatory subject and the other during the middle of pregnancy.

It will be noted further that the graphs present suggestive evidence that certain subjects are completely anovulatory. For example, in Patient 4, the times of the peaks in the cycle are not always consistent. In contrast to the previous study (Burr and Musselman, 1936) where the peaks occurred with astonishing regularity in the middle of the period, the present data show that such regularity is not always present. The graph of Patient 1 is probable evidence of a regular cycle although lack of readings in the first, third, and fourth month at the proper time makes a definite decision impossible. Patient 2 is interesting because the second and third months show peaks immediately after the menstrual period, whereas the last month shows one approximately in the middle. Patient 6 shows two months with peaks in the middle and one with the peak immediately after the period. The graph of Patient 9, which is complicated by an injury to the left hand, shows peaks in the second and fourth months but none in the third which may have been a result of absence. Graph 11 in Fig. 3 shows a peak immediately after the

month under observation, during the first third and last third of the second and third months, and for the fourth month the readings were complicated by injury to the index finger of the right hand. In the first month, Patient 9 gave readings complicated by a traumatized finger in the left hand but in the second and fourth months showed moderate peaks immediately after the menses with no irregularity in the third month, due probably to failure in obtaining regular readings. Patient 11

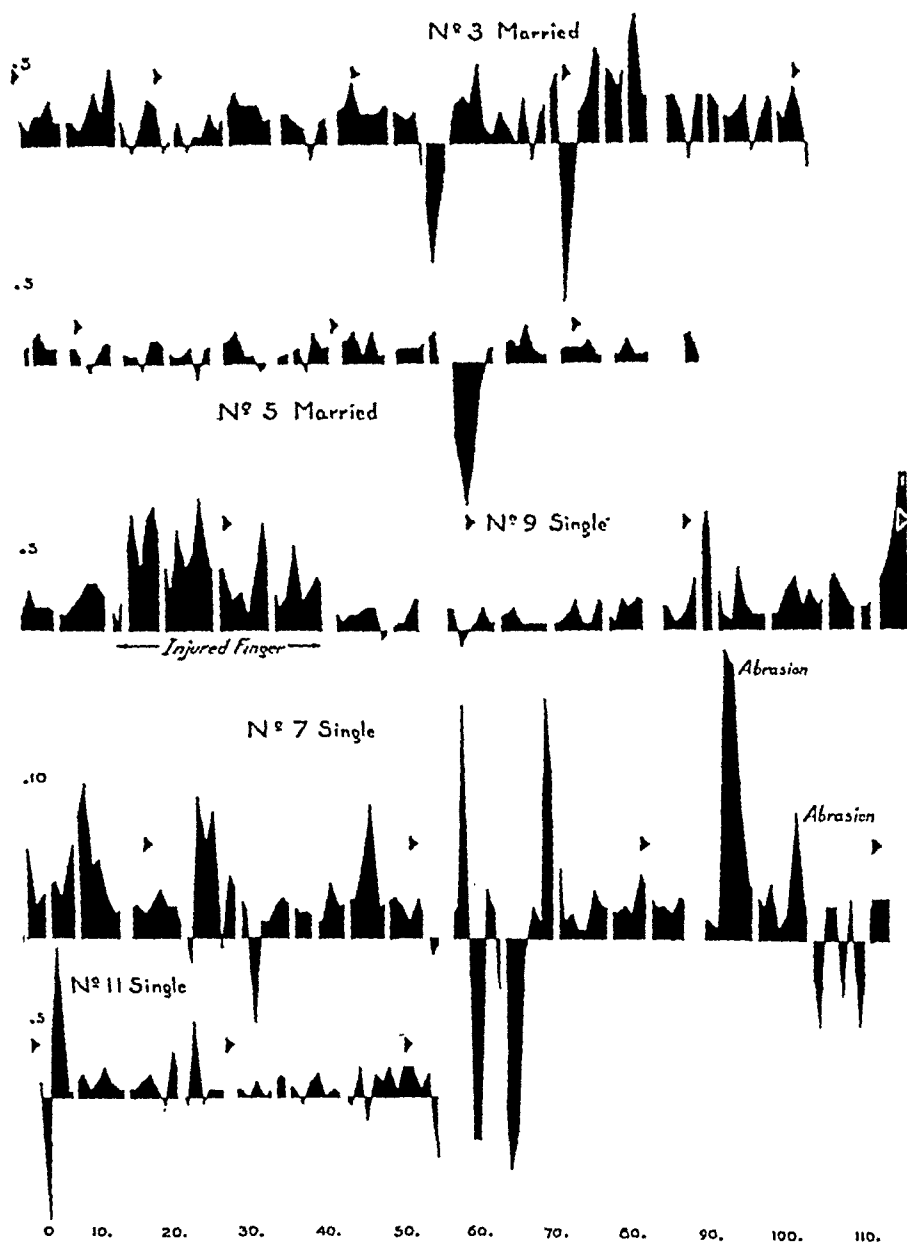


Fig. 3.—Graph showing rises in potential difference chiefly during the few days following menstruation.

showed a marked rise immediately after menses in the first month but none in the second. Patient 3 showed such irregularity as to make classification difficult, as during the third month there was a marked rise at the middle of the period but with a polarity which was reversed with respect to the usual determinations. Patient 5 shows a fairly stable baseline except for the middle of the second period when a marked voltage difference of reversed polarity was observed.

DURATION OF SECRETORY ACTIVITY IN THE GLANDS OF THE DECIDUA VERA*

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WHEN an ovarian cyst is discovered in pregnancy, the question of operation generally arises, and if on exploration the tumor is found to involve the corpus luteum, the surgeon must then weigh the consequences of its excision. It is known that the corpus luteum is essential for implantation, but it has not been definitely established how soon after conception this organ may invariably be dispensed with, in the human being, without interrupting the course of gestation. It was in dealing with this problem that the following study of secretory activity in the glands of the decidua vera was suggested. It was thought that the duration of the response of these glands to the luteal hormone might indicate the period during which progesterin could be considered a physiologic necessity to the life of the fetus.

The possibility of having to remove the corpus luteum occurs whenever a tumor of the adnexa complicates pregnancy. This is not by any means a rarity. From admissions to the Sloane Hospital for Women in New York, Caverly¹ has recorded the incidence of this complication in over 16,000 pregnancies to be 1:500. He reported torsion, hemorrhage, or other acute conditions associated with the cyst itself in 25 per cent of this group and, therefore, advised operation in all cases.

But when a pathologic tumor of the ovary is palpated early in gestation, and when there are no symptoms referable to it, the decision to operate may well depend on evidence indicating when the corpus luteum could, if necessary, be safely excised without risking miscarriage or abortion. Such evidence may be derived from three sources: first, from case reports of successful excision in the literature; second, by analogy from animal experiments, and third, from biologic tests for the presence or absence of the luteal hormone at different stages of pregnancy.

In a review of the literature ten years ago, Ask-Upmark² collected 50 cases of removal of the corpus luteum within the first two months, and of these patients, 33 per cent miscarried. Asdell³ in 1928 reported 38 cases, four of which miscarried. In Caverly's series of 83 cases of ovarian tumor excised during pregnancy, six of the specimens contained the corpus luteum; of these, only the earliest gestation

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period in the first month, a much lower peak at the end of that same period and no peaks in the following period.

While it is possible that ovulation may occur at any time, yet it is highly probable that there are periods entirely without ovulation. Should it eventually develop that the marked bio-electric rises in the voltage difference between the two fingers were correlated with the time of ovulation, the data here presented would indicate that the rupture of the follicle occurs most commonly either in the middle of the cycle or immediately after menstruation. There are no unequivocal cases of peaks immediately preceding menstruation. Furthermore, the data seem to indicate that the cycle is by no means constant in the same individual. Studies are now being undertaken which combine other techniques for the determination of ovulation, and which extend over longer periods of time in the hope that more definite results may be obtained.

Since the above data were collected Burr, Musselman, Barton and Kelly (*Science* 86: 312, 1937) have succeeded in obtaining a continuous graph of the changes in bio-electric potential associated with ovulation in a human being. With one electrode in the vagina and one on the symphysis the record shows a swing of the vaginal potential from a base line of -20 millivolts to +30 millivolts. About twelve hours later, this potential difference increased suddenly, without warning, to about +100 millivolts, throwing the recording mechanism off scale. In fifteen minutes an abrupt drop to 70 millivolts occurred. This was followed fifteen minutes later by another drop to 30 millivolts. At laparotomy, fourteen hours later, the punctate hemorrhage of a ruptured follicle was observed and the corpus luteum excised. Microscopic examination shows a well marked corpus hemorrhagicum and a clearly defined corpus luteum. This observation gives weight to the bio-electric data described above, since it indicates that in a human being, as in the rabbit, ovulation is accompanied by voltage surges of considerable magnitude.

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been cast off. By the second week after this bleeding started, the simple, tubular glands begin to show prolific mitotic activity in their columnar epithelial cells, and as a result they become greatly elongated, coiled, and twisted when seen in longitudinal section. The nuclei of these gland cells are tightly packed, long, narrow, and deeply stained through the first, or preovulatory half of a normal cycle. At about the fifteenth day, or soon after, ovulation occurs, and it is then that the elaboration of progestin brings about significant changes in the glands and epithelial cells; mitotic growth ceases and secretion begins. The glands become "saw-toothed," and are lined with swollen cells containing round, basal, clear-staining nuclei. Before menstruation the epithelium is cuboidal and secretory discharge distends the gland lumen. This modification into a secretory tissue is so clear-cut that there is generally little difficulty in demonstrating by these

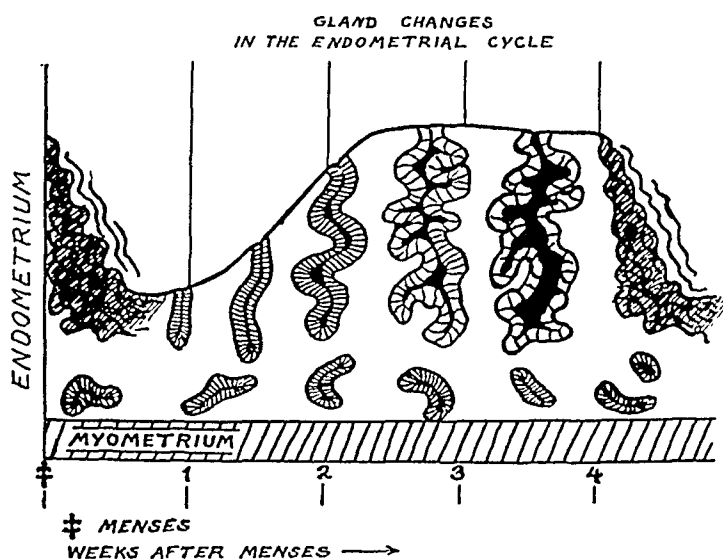


Fig. 1.

changes the presence of an actively functioning corpus luteum. It should be noted that throughout the normal cycle the basal glands, that is, the glandular roots lying near the myometrium, take no part either in proliferative activity or secretory discharge; throughout the month they remain static, inert. If the egg is not fertilized and implanted, then coincident with corpus luteum atrophy, the endometrium again breaks down in the next menstrual flow.

If, however, a fertile egg is implanted, the corpus does not involute but continues to grow and expand. The endometrial glands of early pregnancy reflect this continuation of progestin output by even more marked secretion than that seen during the preceding two weeks.

To study the duration of this secretory activity, surgical specimens of 13 uteri were selected with the object of observing such activity at approximately three-week intervals through pregnancy. None of these

at two months was interrupted. We have recently seen three cases in this hospital;* in two, the operation was done eight weeks after the last menses, and they both miscarried on the fifth and ninth day postoperatively. The third pregnancy, one of ten weeks, was not disturbed by removal of a large lutein cyst. There are numerous reports of isolated cases of this procedure scattered through the recent literature, but interpretation of this evidence is difficult. It has been pointed out³ that most of the cases have been recorded simply because a viable baby was obtained in spite of unilateral or bilateral oophorectomy, yet it is probable that a great many similar operations resulting in miscarriage never have appeared in print. Many of the authors do not always explicitly state that a retained ovary was even visualized, and it is impossible to be certain that all luteal tissue has been removed in such reports. The factor of trauma incident to the operation varies widely in the hands of individual surgeons, yet may at times play a part in subsequent miscarriage. Unfortunately, there has never been, and probably never will be, a large series of consecutive cases of removal of the corpus luteum in different stages of gestation, carefully controlled and reported in detail by one man; the reason is obvious. The case reports that are available merely suggest that after the second month the corpus luteum may often, but not always, be removed without interrupting pregnancy, whereas before the second month such an operation seems to result in from 10 per cent to 33 per cent of miscarriages. More definite conclusions are hardly justified because of the above considerations from the data in the literature alone.

Animal experimentation has demonstrated a species variability in the dependence of successful gestation on the corpus luteum. Thus, the goat and opossum, squirrel, mouse, and bitch⁴ will almost invariably miscarry after double ovariectomy at any stage of pregnancy. The rabbit will always miscarry if operated upon within eight days of mating, and generally at any subsequent time before term.^{5, 6} The guinea pig, however, will generally carry through such a procedure without interruption, if it is done more than two days after conception.⁷ But the results of these investigations cannot reasonably be applied to the same problem in the human species.

From biologic tests for the presence of progesterin through pregnancy one might hope to show the duration of the physiologic activity of the corpus. Unfortunately, the hormone seems to be in such low concentration in the circulation that it has thus far not been recovered in blood or urine. Such a possible test would be further complicated by the demonstrated presence of progesterin in placentae during the latter months of pregnancy.^{8, 9} The assay for this hormone in human ovaries removed at different intervals after conception has not been done. There remains as a possible test of the life of the luteal body, a study of the duration of the characteristic response to this stimulus of the endometrial glands in the decidua vera.

The typical features of endometrial response to progesterin are seen in the latter half of a normal menstrual cycle (see Fig. 1). In the preceding menstrual flow, the upper two-thirds of the mucous membrane lining the uterine cavity is shown, diagrammatically, to have

*Brief protocols are included at end of paper.

Fig. 2, from a six weeks pregnant uterus, shows a gland from the basal layer, embedded in muscle tissue. The nuclei are long, narrow, deep-staining, in high columnar epithelial cells. Although glands in the upper layers of the decidua show

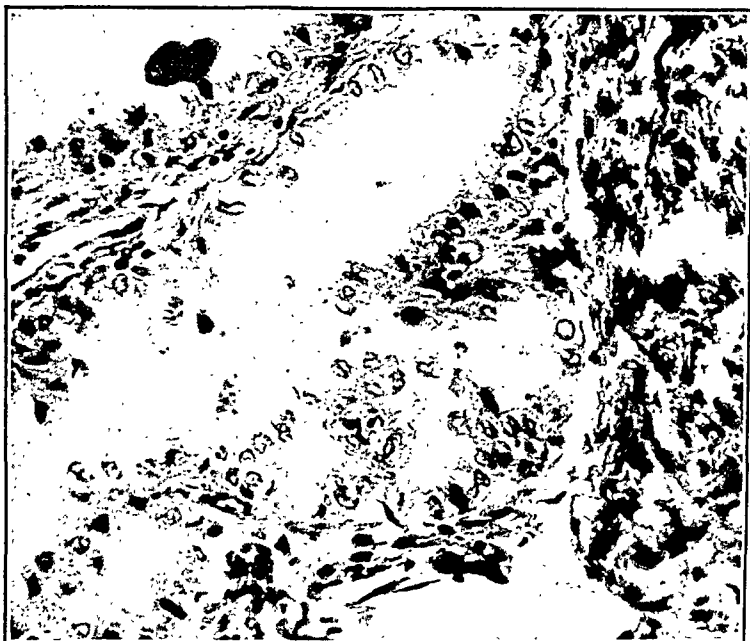


Fig. 4.—Eighteen weeks' pregnancy; a decidual gland from the basal layer showing evidence of active secretion. (Case S-36-498.)

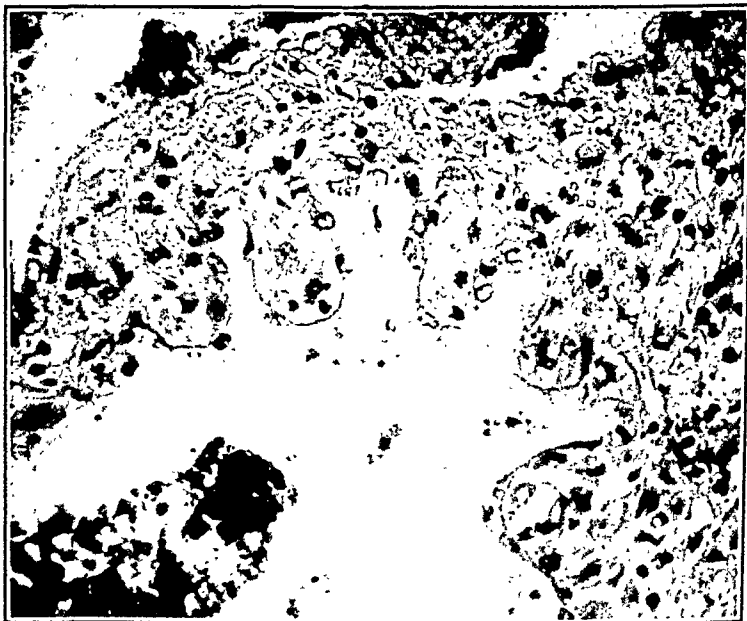


Fig. 5.—Twenty-three weeks' pregnancy; a decidual gland from spongy layer. The cells lining this gland are losing their epithelial characteristics. The lumen contains masses of cellular debris. (Case S-35-909.)

active secretion at this stage, there is here seen no evidence of any activity in the basalis glands.

A gland from the middle or spongy layer of a ten weeks decidua is seen in Fig. 3. The epithelial cells are cuboidal and contain round clear nuclei. The luminal

specimens had been removed for local pathology that could have influenced the histologic appearance of the glands in the decidua. Specimens from both decidua vera and the decidua basalis were in most

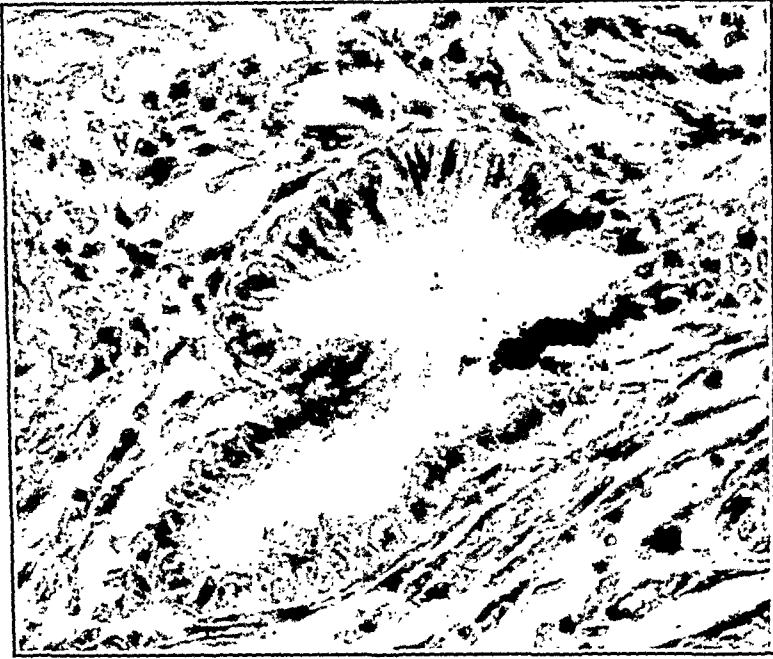


Fig. 2.—Six weeks' pregnancy; a decidual gland from basal layer showing neither proliferative nor secretory activity. Except where stated, these photographs are all from decidua vera. (Case S-36-753.)



Fig. 3.—Ten weeks' pregnancy; a decidual gland from spongy layer beneath implantation site. The cells are cuboidal, the nuclei round; this gland is in active function. (Case S-35-658.)

cases available. Photographs were made from some of these sections to demonstrate the progressive changes occurring in the glands during pregnancy.

the clear, swollen cells with round nuclei are seen bulging into the lumen. It is of interest that the modification of the inactive basal glands shown in Fig. 2 into the functioning structures seen in Fig. 4 takes place without any demonstrable intervening phase of mitotic proliferation.

A gland from the spongy layer at twenty-three weeks is reproduced in Fig. 5. Here the gland lining is gradually losing its epithelial characteristics. These cells are thinning out, in places they are entirely missing, leaving the decidual stroma denuded. The large sinusoidal spaces that were once gland lumina are filled with debris, partly from infiltrating blood elements and partly from the degenerating epithelial margins.

At thirty-two weeks, this process of degeneration has progressed still further. In the upper decidual layers, the irregular spaces have almost the appearance of thin-walled lymphatic sinuses lined in places with endothelial-like cells (Fig. 6). It is only by tracing the glands from early pregnancy that one can confidently recognize

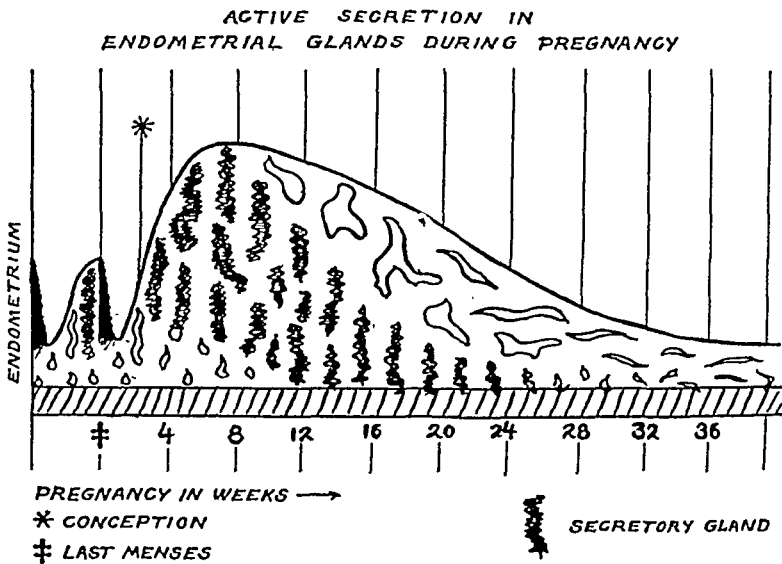


Fig. 8.

them as the origins of the spaces seen at eight months. In the basal layer (Fig. 7), at the same time, there is found no evidence of active function, and the cells lining the gland are apparently being cast off into the lumen.

The duration and extent of active secretion in the decidua vera as demonstrated in Figs. 2 to 7 is summarized in Fig. 8. At eight weeks there is found the greatest extent of activity in the upper layers of the decidua, though the basal glands have not undergone any changes. Beginning nearest the surface and gradually extending downward, there is a loss of glandular secretion shortly after the second month, and a coincident degeneration of the glands into large sinusoidal spaces. At the same time, there takes place a progressive functional involvement of the basalis layer. At the fifth month, only the gland structures near the myometrium show any activity, and by the seventh month all evidence of secretion is lost. It will be noted that the glands of the upper superficial layer, those nearest the surface and therefore, perhaps, most important in any function concerning a newly-planted embryo, lose their activity about two months from the previous menses. It is also seen that the basal glands generally exhibit no significant activity except from about the twelfth to the twenty-fourth week of pregnancy.

margin is indistinct and frayed. This section was from the implantation site, and the gland lumina are markedly swollen with secretion, possibly due to obstruction of the gland mouths by the growing trophoblast above. It may be this distention

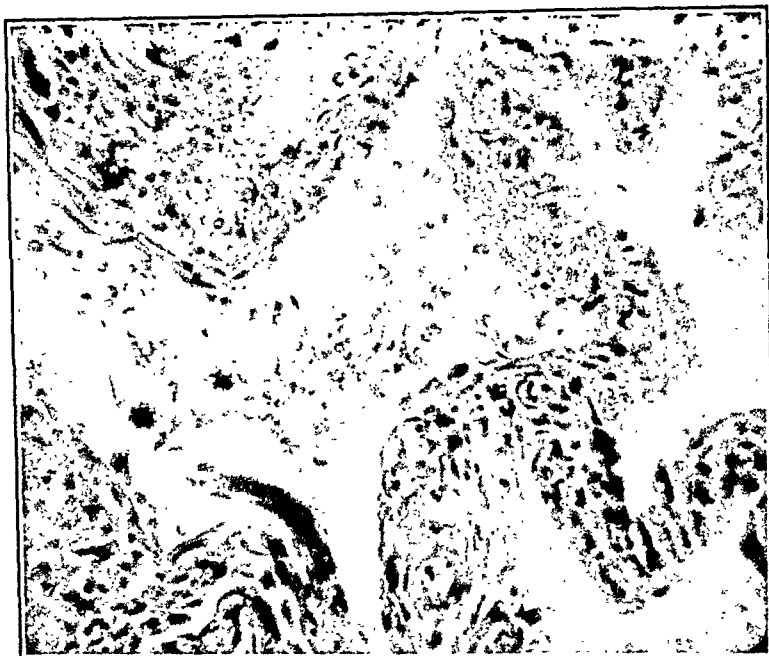


Fig. 6.—Thirty-two weeks' pregnancy; a decidual gland from spongy layer which has degenerated into a large irregular sinusoidal space containing blood cells and epithelial debris. (Case S-34-135.)

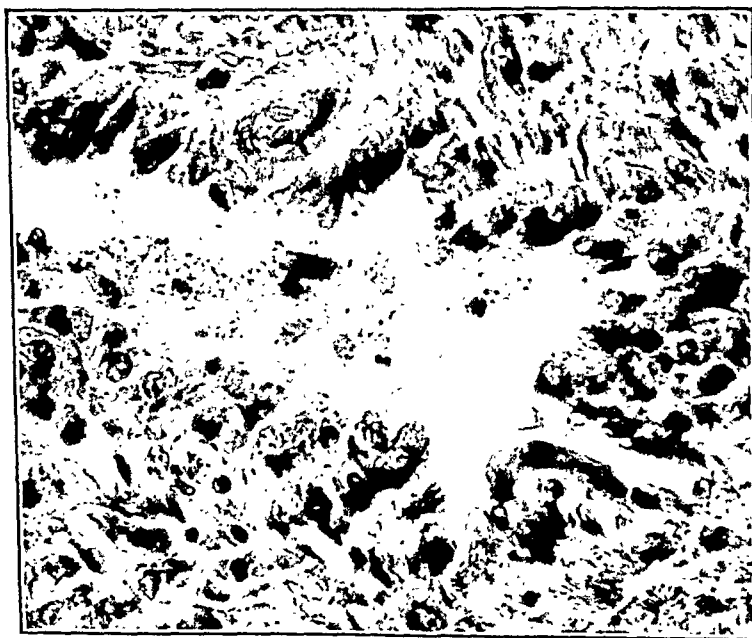


Fig. 7.—Thirty-two weeks' pregnancy; a decidual gland from basal layer showing degenerative changes. (Case S-34-135.)

that causes the lining epithelium to appear so flattened, but the cytology is definitely that of active secretion.

In Fig. 4, a gland from the basal layer, resting on muscle bundles, is again shown, from an eighteen weeks' pregnancy. At this stage these glands are secreting actively;

standing of the risks of removing the corpus luteum in early gestation. The characteristic response of decidual glands to progesterin is the only available test, at present, for this hormone. The duration of this response was studied in specimens of uteri removed at approximately three-week intervals through pregnancy.

CONCLUSIONS

1. The nature of the secretory response seen in the decidual glands suggests that the duration of this activity cannot lead to positive conclusions concerning the length of functional life of the corpus luteum of pregnancy.

2. The maximum involvement of decidual glands in active secretion is found at about the eighth week in the most superficial zones of the decidua vera. This would appear to lend a certain amount of support to conclusions from evidence in the literature, that the corpus luteum cannot be excised within eight weeks from the last menses, without seriously jeopardizing the successful course of gestation.

PROTOCOLS

M. G. H. (Case 14390), married, aged 29 years, para iii, housewife, last menses Apr. 28, 1936. She was first seen June 21, 1936, complaining of steady low abdominal pain two weeks. She showed large retroverted uterus, and cyst in the right ovary. Operation June 22, 1936. A two months' pregnant uterus was left untouched. Large cyst right ovary necessitating removal of whole organ. Corpus luteum in cyst wall. Left ovary small, scarred, no corpora lutea. *Pathologic Report*: Lutein cyst. Following operation very slight amount of staining with mild cramps and clots June 25, 1936. This continued with passage of decidua and clots until July 1, 1936, when miscarriage apparently was completed, and from then on convalescence was uneventful.

P. H. (Case 31038), married, aged 29 years, housewife, one child, one miscarriage. Last menses Oct. 14, 1936. Seen Dec. 9, 1936, complaining of vague abdominal discomfort. Had had slight staining off and on for three weeks. Uterus definitely enlarged, cyst in right vault size of orange. Operation Dec. 10, 1936; two to three months pregnant uterus left untouched. Large cystic right ovary. Fluid aspirated and cyst wall resected. Left ovary inactive with neither follicles nor corpora lutea. *Pathologic Report*: Lutein cyst. In spite of 4 rabbit units of proluton on December 11 and December 12, patient bled freely with cramps on December 15; abortion then considered inevitable and curettage done Dec. 15, 1936, with uneventful convalescence.

B. M. (Case 16893), single, aged 21 years, student, examined Jan. 9, 1935, found to have uterus size of two and a half to three months' pregnancy. Right adnexa normal; left, definite mass 2 inches to 3 inches in diameter. History of introduction of blunt instrument two weeks before followed by slight bleeding for a few days. Exact date of last menses not known. Jan. 11, 1935, operation, normal pregnancy of at least two and a half months, uterus left untouched. Left ovary showed bilocular cyst size of a lemon; right ovary showed many follicles and old scars, no corpora lutea. Left ovariectomy performed. *Pathologic Report*: Follicle and lutein cysts. Course: normal postoperative recovery, but three weeks after leaving hospital and five weeks post-operatively, patient reported that she miscarried.

DISCUSSION

The progressive nature of the glandular involvement demonstrated in this study is difficult to explain on the basis of variations in hormone stimulus alone. The character of the response in the decidua glands suggests that duration of secretion does not accurately reflect the length of life of the corpus luteum of pregnancy. The degeneration of these glands, appearing in those that react first and passing down to those influenced last, implies that their secretory function is limited perhaps by some factor intrinsic to the glands themselves rather than by a decrease in the stimulating mechanism. Thus, Hisaw¹⁰ has described as an exhaustion phenomenon the involution of secretory glands in a castrate *Macacus rhesus* after twenty-four days of constant progestin administration. It is possible that the duration of secretion in the decidua vera is terminated by a similar "exhaustion" of the glands. Since progestin has been recovered from placentae at term where it is presumably available as a source of stimulus, the "exhaustion" hypothesis would explain the lack of any apparent secretion in the decidua at that time.

The secretory changes here studied are histologically similar to those resulting from response to progestin alone in an estrin-primed endometrium.¹⁰ There is scant evidence that these changes can ever be maintained for weeks by progestin and estrin alone, from a "persistent luteoma," except in gestation. Since it is normally only in pregnancy that the pregnancy urine hormone (anterior pituitary-like hormone) is available to the organism, it is possible that this stimulus plays a part in the secretory response of the glands. It may be significant that recent quantitative assays for the pregnancy urine hormone¹¹ have shown a peak at the eighth week, with a gradual decrease to a considerably lower plateau thereafter. Although the addition of pregnancy urine hormone perhaps makes possible a longer glandular response than that which could be obtained without it, yet the decrease of pregnancy urine hormone after the eighth week does not necessarily explain the progressive quality of the glandular response described in this study.

SUMMARY

When pregnancy is complicated by an ovarian tumor, operative removal of the tumor may involve the corpus luteum. Evidence from the literature suggests that excision of the corpus luteum results in from 10 per cent to 33 per cent of miscarriages if done within the first two months. This evidence, however, is neither statistically accurate nor reliable. If a satisfactory test for the presence of the luteal hormone could be devised, it might be possible to determine the length of functional life of the corpus luteum. This would lead to a better under-

preparation of the hypophysis prophylactically, in two series, and no oxytocic in the third, concluded that the routine prophylactic injection offered no real advantage in the majority of cases. The more recent studies of Scott (1925) and Jess (1926) concerned pituitary and nonpituitary series and were distinctly in favor of prophylactic administration.

Today it is an accepted fact that posterior pituitary extract reduces the postpartum blood loss, but the question is whether the early prophylactic administration is more advantageous than administration immediately following labor, and even whether it is not actually detrimental. A careful search of the literature has not revealed a single comparative study on the point in question. This is indeed surprising in view of the lack of agreement from authoritative sources. DeLee recommends it following the birth of the baby "where ideal maternity conditions are available." Davis and others believe that the third stage is shortened and hemorrhage decreased by early administration but state that "the use of posterior pituitary extract should be confined to Hospital practice, where complications of the third stage can be more safely managed than in the home." The late J. W. Williams always believed that "the excessive contraction as occasionally induced by solutions of pituitary is potentially productive of real pathologic changes." Calkins definitely states that it should be given "immediately after the delivery of the placenta, never before, because the constant (physiologic) contraction is necessary during the separation phase of the third stage." Urner believes the early administration of pituitrin "plays an important part in lessening the blood loss" and believes that the objection on the basis of hour-glass contraction is theoretical, "as this condition has not occurred with any greater frequency in a similar group of patients where no pituitrin was used after the first stage of labor."

I am herewith reporting the results of a comparative evaluation of a solution of the pituitary given at the onset and after the completion of the third stage of labor.

THE PRESENT STUDY

Over a period of thirteen months, we have administered 1 c.c. of a physiologically tested and standardized solution of the hypophysis containing 10 international units routinely by hypodermic injection, to 1,100 consecutive full-term and premature vaginal deliveries at the onset of the third stage of labor; we compared the results with a similar series in which the patients received the same medication immediately following the completion of labor. The oxytocic fraction (pitocin) was substituted in cases presenting a contraindication to the use of a solution of the whole posterior lobe, and solutions of ergot were used as indicated to control hemorrhage.

From Jan. 11, 1936, to Feb. 12, 1937, 2,340 women were delivered in the Lewis Memorial Maternity Hospital. Four maternal deaths occurred, hence the uncorrected mortality was 0.17 per cent. Expressed in terms of live births this was 0.177 per cent or 1.77 per thousand. For reasons stated further on, only one death is included in this series and that was the result of a postpartum hemorrhage. The uncorrected infantile mortality was 3 per cent.

This study was made possible by the generous help and sympathetic cooperation of Drs. Arthur Hertig and Hugh Nuckols who placed material from the Pathology Laboratory of the Boston Lying-in Hospital at the author's disposal.

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A COMPARATIVE STUDY OF POSTERIOR PITUITARY EXTRACT ADMINISTERED AT THE ONSET OF AND AFTER THE COMPLETION OF THE THIRD STAGE OF LABOR

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THE active principle of the posterior lobe of the hypophysis cerebri, commonly called pituitrin, was introduced into the practice of obstetrics in 1909 by Blair-Bell. This innovation failed to attract much attention at first, but was generally adopted in 1911 following the studies and recommendation of Hofbauer. In the voluminous literature which followed here and abroad, we find occasional references to the advantages of using this oxytocic at the onset of the third stage of labor. This so-called prophylactic administration was cautiously introduced in anticipated postpartum hemorrhages, e.g., in hydramnios, following the delivery of twins or excessive babies, etc. As early as 1913, we read that Teufel and Rübsamen, independently and in the same year, administered this new oxytocic as the baby's head was being delivered. The latter reported a reduction to one-third or one-fourth of the average blood loss.

Fellenberg, in 1914, brought the subject of prophylactic injection of the infundibular extract to the attention of the Gynecological Congress in Berne, and seven years later having used it routinely in this manner reported favorable results and advocated its prophylactic administration. In the same year (1921), Ryder administered the drug to 100 patients following the completion of the second stage of labor, and compared the results with an equal number of patients who did not receive an oxytocic. The conclusion reached was that this early administration "appeared to be safe and valuable in minimizing the blood loss." The following year Broadhead and Langrock corroborated the results in a similar series. Several other studies of the same nature appeared in the literature during the ensuing years. A dissenting voice was, however, heard during this wave of enthusiasm. Reist and Guggenheim, in 1923, after comparing three series each of 100 cases and using a different

involved, a difference in technique of management of the third stage, the training and experience of the attending personnel, the type of patient, and what is perhaps most important of all, a difference in the method of measuring the blood loss. More uniform results would unquestionably be reported were a uniform method of measuring adopted. This, I believe, is well brought out in the present report.

The technique of measuring the postpartum blood loss in this study was developed in the Lewis Memorial Maternity Hospital and is based on the principle proposed by Pastore, whereby the blood is collected

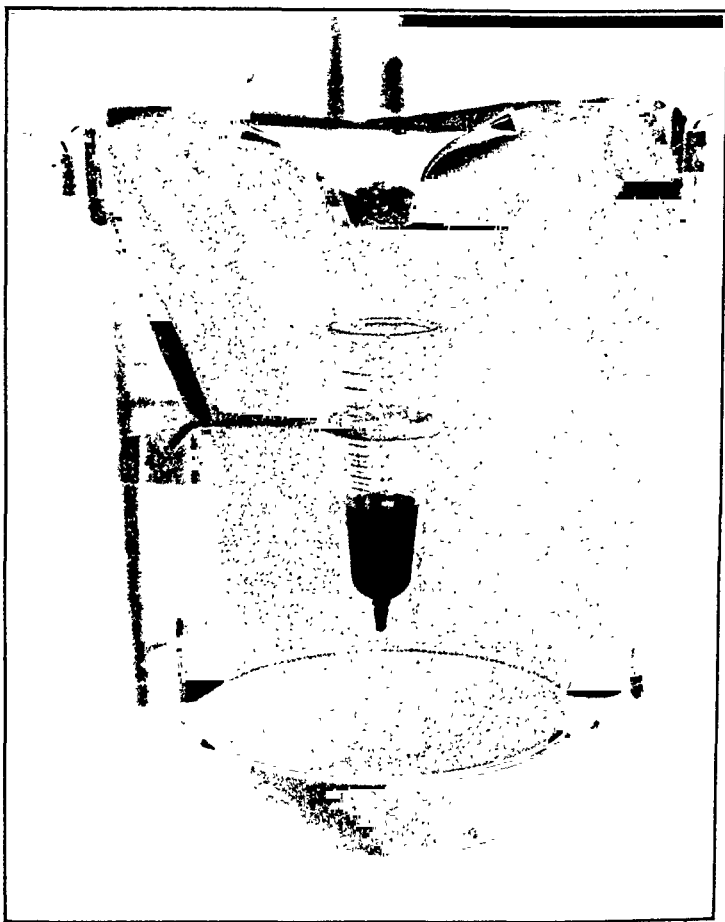


Fig. 1.—The sterile chrome plated pan and trough directs the blood stream downward. The graduated glass collector is moved in or out of range of the flow by pressing the left knee against the projecting bar.

and the amount read at a moment's notice throughout the third stage of labor, including when necessary the blood lost just prior to delivery from a laceration or episiotomy, and excluding nonsanguineous flows such as amniotic fluid, urine, or antiseptic solutions. The apparatus has been greatly simplified without impairing its accuracy. Whereas Pastore deflected the flow of amniotic fluid by a movable trough attached to the collecting pan, we eliminate that by moving the graduated glass collector out of range of the flow. The deflection is effected at a moment's notice by knee action and a reading is possible at any

Subtracting 27 patients delivered by cesarean section (an incidence of 1.1 per cent), and 28 whose babies weighed less than 1,500 gm. or measured less than 35 cm. in length, there were 2,285 full-term and premature vaginal deliveries. Eighty-five of these cases were not included in the study, because the blood loss was not measured or was inaccurately measured. In the nonmeasured or estimated group, there are included all patients delivered on the "septic floor" on which there was no equipment to measure blood, and the occasional precipitate deliveries. Inaccurate measurements resulted when unruly patients were delivered, or the attendant did not eliminate amniotic fluid, etc., or failed to collect all the blood. In this group the blood loss was sufficient in 7 cases to be classified as a postpartum hemorrhage, and the placenta was removed manually in 3 cases.

Thus 2,200 full-term and premature vaginal deliveries constituting 96 per cent of all deliveries in this class, over a period of thirteen months, offered material for analytical study. All patients were delivered by the resident staff and the obstetrician-in-chief. All but the more difficult operative cases were attended by young men (junior residents) who were starting to learn the principles of obstetrics. Two different groups cooperated in the study, and in order to make the comparison more valid, each group delivered approximately one-half the total number of patients in each series. It has been our custom to use as little analgesia as possible. In some cases morphine and a derivative of barbituric acid were given during the first stage, and all patients were delivered under ether, ethylene, or chloroform anesthesia.

The technique of management of the third stage as advocated by Calkins was adopted *in toto*. To quote: "Immediately after delivery of the baby, the hand is placed on the abdomen; the uterus is held very gently with the fingers behind and the thumb in front, and with no attempt to massage the organ unless it shows signs of relaxation and flaccidity. As soon as it changes from a discoid to a globular shape, and a trickle of blood appears from the vagina, the organ is vigorously massaged until it becomes firmly contracted and then, by squeezing and gentle downward pressure an attempt is made to express the placenta. Should the placenta not come out readily, no further attempt is made to express it, and no further massage is instituted until some sign of enlargement or flaccidity appears or there is an increase in bleeding from the vagina. Immediately after delivery of the placenta the uterus is again massaged to obtain firm contraction, and the hand is kept constantly in contact with the uterus for a period of one hour or until such time as the attendant assures himself that there will be no further tendency toward relaxation or flaccidity."

There is a wide difference in reports on postpartum blood loss from various representative clinics. A number of factors are undoubtedly

If we arrange the total blood losses in groups of 100, starting at zero or at 50 c.c., and compare the group incidence, there is a striking similarity of distribution as seen in Figs. 2 and 3. The difference in the general average is negligible; it was 5 c.c. less in the series receiving the oxytocic prophylactically. The averages were 270 c.c. and 275 c.c.

The previous comparative studies involving prophylactic pituitary and nonpituitary series have shown a considerably greater advantage of the former. As before mentioned Rübsamen reduced the average loss from 300 c.c. to between 75 and 100 c.c., a reduction of 66 to 75 per cent of the average blood loss. Ryder using Williams' technique of measuring the blood loss, in a series of 200 cases demonstrated a reduction of $2\frac{1}{3}$ ounces (70 c.c.), the averages being 5.9 ounces (177 c.c.) and 8.2 ounces (247 c.c.), a reduction of 30 per cent on the average. This study was corroborated by that of Broadhead and Langrock. Reist and Guggenheim denied the advantages heretofore demonstrated, claiming that in general the blood loss was unaffected by the prophylactic injection of pituitary. However, they maintained that it did lessen the blood loss in cases of atonia uteri, especially when associated with deep anesthesia and in repeated postpartum hemorrhages, in which cases only did they believe it was indicated. Scott's figures showed a reduction of 20 per cent of the average loss, a saving of 44.8 c.c., the average being 198.7 and 243.5. Using pituitrin prophylactically and intravenously Jess reported a saving of nearly one-half the average blood loss in normal and operative cases: his figures were 398.2 reduced to 187.8 c.c. and 655 reduced to 342 c.c., respectively.

In comparing our results with those already reported, the importance of a uniform method of measuring the postpartum blood loss is evident. Pastore reported an average blood loss of 244.3 c.c. in a series of 574 cases, as compared with our 275 c.c. In 70 per cent of his patients the blood loss was less than 300 c.c. as compared with 69.8 per cent in our series. In a later study he reported an average loss in 1,870 deliveries of 271.3 c.c. The average loss reported in the literature ranges from 179 c.c. (Calkins) to 500 c.c. (DeLee, Ahfeld, Sellheim). Tarnier's average of 600 c.c. is perhaps the highest on record. In Williams' clinic the average in 1,000 spontaneous deliveries was 343 c.c., and Plass using the same technique in a series of private cases reduced it to 317. The reduction is attributed to management by the experienced obstetrician in contrast to the young apprentice.

Calkins who is strongly in favor of administering pituitary solution only after the placenta has been delivered, reported an average blood loss of 222 c.c. and later with an improved technique in the management of the third stage (which we have adopted) reduced it to 179 c.c. with

time. Fig. 1 shows one of three such blood measuring set-ups used in this study. In delivering each patient special attention was paid to (1) accurate measurements of postpartum blood loss, and (2) correct timing of the duration of the third stage of labor. Manual removal of the placenta was resorted to for strict indications only.

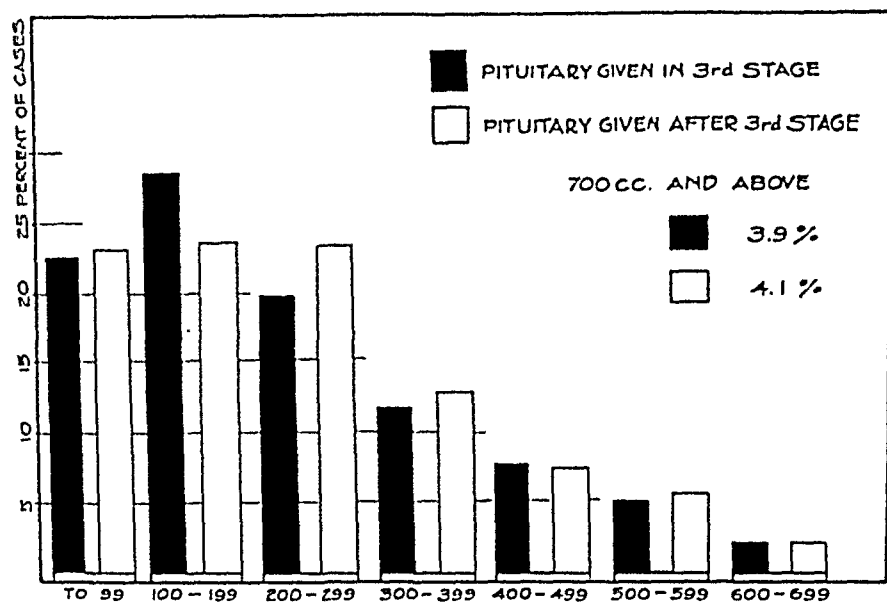


Fig. 2.—Blood loss in 100 c.c. groups.

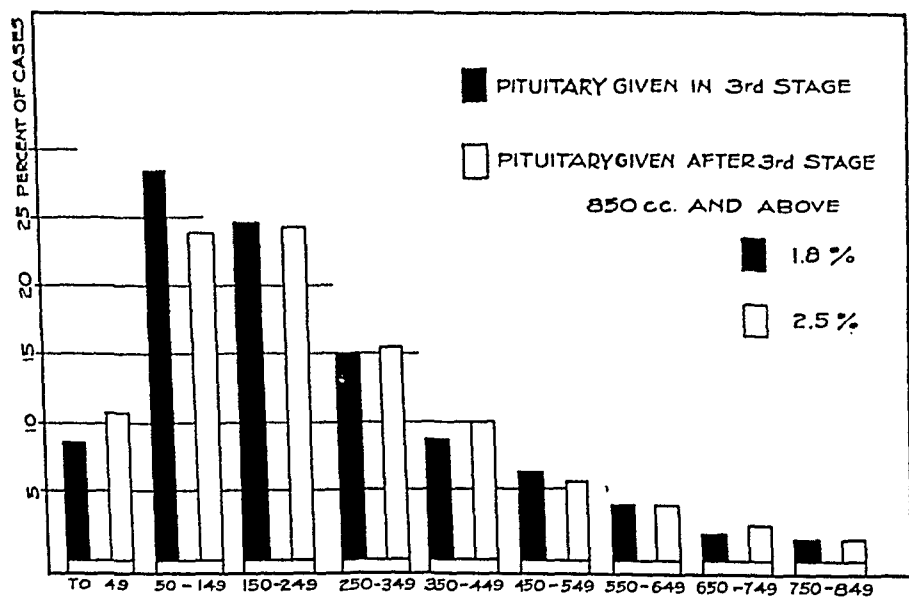


Fig. 3.—Blood loss in 100 c.c. groups.

COMPARATIVE RESULTS

The postpartum blood losses here reported are total losses for the period during which the patients remained on the delivery table, a minimum of one hour. The clots expressed during or at the end of that period are included. As a result, a considerable number of total losses were increased in amount.

favorably with that of Pastore (6.4 per cent and 7.11 per cent in a later report), and of Peckham and Kuder (6.14 per cent). It is one-half that of Williams (13 per cent), less than that of Plass, and about twice as great as that of Calkins (2.5 per cent) and Urner (3.4 per cent).

TABLE III. HEMORRHAGES GROUPED AS TO CAUSES

	ATONY		MISMANAGEMENT		VARIOUS		HOURGLASS CONTRACTIONS
	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	
Pituitary before	35	50.7	24	34.7	9	13.0	1
Pituitary after	33	50.0	23	34.8	9	13.8	1

The results of an analysis of causative factors in Table III, show that the prophylactic administration of pituitary does not influence postpartum hemorrhages from an etiologic standpoint. The group termed atony includes cases of hydramnios, twin births, excessive sized babies, atony due to deep anesthesia or prolonged labor, as well as the primarily inactive uterus. If the prophylactic administration of pituitary extract has any value in reducing postpartum blood loss, it should certainly be evident in this group. Comparing the average blood loss in each series we find that the earlier administration reduces the hemorrhage from 1,060 to 885 c.c., a saving of 175 c.c., or 16.5 per cent.

The mismanagement group, referred to in Table III, includes cases having a major portion of the bleeding with expulsion of the placenta and those in which the placenta was prolapsed into the hollow of the sacrum. Cervical lacerations, deep vaginal tears, ruptured varicosities, retained cotyledons, and myomata uteri are grouped under "various."

Impressed by reports of Moir, Dale, Davis, Adair and others, we used ergonovine to control hemorrhages, giving 0.25 mg. intravenously. We have not witnessed any untoward reactions attributable to this drug. The prompt and lasting uterine response with resulting control of the hemorrhage has indeed been most gratifying. It was used in approximately one-half of each series, and following its introduction uterine tamponade was found necessary in only 0.23 per cent of cases as compared with 1.1 per cent before its introduction. The incidence of packing was therefore reduced 79 per cent.

The drug, however, was administered, but to no avail, in the fatal postpartum hemorrhage occurring during this study. A summary of the sequence of events in this case will now be presented.

M. W., a 33-year-old para iv, gravida vi, had an uneventful obstetric history. The physical examination was entirely normal except for moderate sized varicosities of

89 per cent of the total losses below 300 c.c. His technique of measuring, as described in an earlier paper, includes estimation as a part of the total loss and, of course, introduces the personal element. In Uner's series of more than 7,500 cases in which pituitrin was given at the onset of the third stage, 86.9 per cent lost less than 300 c.c., but nothing was said of the method used in measuring the blood.

In Table I, the average results of spontaneous and induced labors are shown but are difficult to interpret. The majority of these cases were merely stimulated with oleum ricini and quinine during the course of a desultory labor. Those induced with solutions of pituitary

TABLE I. AVERAGE BLOOD LOSS IN RELATION TO TYPE OF DELIVERY

TYPE	PITUITARY EXT. BEFORE		PITUITARY EXT. AFTER	
Spontaneous		269 c.c.		277 c.c.
Induced	9%	288 c.c.	7.0%	261 c.c.
Normal		249 c.c.		264 c.c.
Operative	10%	423 c.c.	9.1%	450 c.c.

extract or by surgical means are included, but are too few to permit any conclusions. In the table, we see that induced and stimulated labors bled more than spontaneous labors when pituitary extract was given prophylactically, and less when it was given at the end of labor. The results appear inconsistent. In comparing normal and operative deliveries there is a small but constant advantage in the prophylactic administration. In normal deliveries 15 c.c. were saved and in operative 27 c.c. Analgesia in the form of barbituric acid derivatives administered during the first stage has, in our experience, increased the blood loss. In 200 cases the average blood loss was 295 c.c. and the incidence of hemorrhage was 7.4 per cent. This is more than 1 per cent higher than the general incidence of hemorrhage to be reported.

As suggested by Williams a total blood loss of 600 c.c. or more is considered abnormal, and classified as a hemorrhage. As seen in Table II, the prophylactic administration of pituitary extract reduced the hemorrhage by only 0.27 per cent. The average loss was reduced only 5 c.c. This, of course, is not a fair evaluation of the efficacy of pituitary extract, inasmuch as it cannot be expected to affect a hemorrhage resulting from a laceration, ruptured varix, etc. We shall return to this point in an analysis of hemorrhages in relation to causative factors. Our incidence of postpartum hemorrhage compares

TABLE II. EFFECT OF PROPHYLACTIC PITUITARY EXTRACT ON HEMORRHAGES

	NO. OF HEM- ORRHAGES	PERCENTAGE	AVERAGE LOSS
Pituitary Ext. before	66	6.0	837.4 c.c.
Pituitary Ext. after	69	6.27	842.5 c.c.

Fig. 4 shows the distribution of cases according to the time of separation and expression of the placenta, which using the Calkins technique should be practically simultaneous.

TABLE IV. BLOOD LOSS IN RELATION TO TIME OF PLACENTAL SEPARATION

	UP TO 2 MINUTES			3 TO 5 MINUTES			6 TO 10 MIN.			ABOVE 10 MIN.		
	NO.	%	AV.	NO.	%	AV.	NO.	%	AV.	NO.	%	AV.
Pituitary Ext. before	170	15.4	258.9	729	66.2	264.0	171	15.5	252.7	30	2.7	358.9
Pituitary Ext. after	163	14.8	272.0	615	55.9	258.6	260	23.6	294.0	62	5.6	387.3

There is a remarkable parallelism between the two curves, except at the points three and four minutes where a deviation is evident. It is clear that prophylactic pituitary causes 11 per cent more of the placentae to separate within four minutes, and this advantage (if it is an advantage) is practically confined to the three- and four-minute periods. It is, therefore, clinically evident that in the immediate postpartum period the infundibular extract acts in three to four minutes. It is generally believed by the proponents of prophylactic pituitary administration that the third stage is shortened and the blood loss thereby decreased.

A careful consideration of Table IV shows that the average blood loss is considerably increased, about 100 c.c. on the average when the placenta is retained over ten minutes. Of course in these cases, the bleeding episiotomy wound increases the total to some extent. The prophylactic administration reduced the incidence of such cases 2.9 per cent, and reduced the total blood loss by 29 c.c. or 7.5 per cent of the average loss. We may also assume that 8.1 per cent of the cases had a shorter third stage than six to ten minutes due to the early administration of pituitary extract, and the average blood loss was reduced 14 per cent. Below five minutes the prophylactic administration series includes 11 per cent more cases than the group in which pituitary was given after expulsion of the placenta. In this same group the difference in blood loss is not large enough to be significant, bearing in mind that the fatal hemorrhage undoubtedly accounts for the higher figure in the group termed "up to two minutes."

It would seem therefore that the optimum time for the separation and expression of the placenta is before five minutes, and while the earlier administration of pituitary extract does not lessen the bleeding in this group, it places 11 per cent more cases in the group. When the duration is longer than five minutes, prophylactic administration is effective in reducing the blood loss.

A comparison of the complications of the third stage of labor as shown in Table V might be interpreted as slightly in favor of the

both legs. The pelvis was normal, blood Wassermann negative and hemoglobin 80 per cent. The antenatal course was normal in every way. She was admitted in very mild labor one week after the expected date of confinement, and on admission a definite hydramnios was noted. Seven hours after admission she was given 3 gr. of quinine bisulphate for three doses at half-hour intervals. Twenty-four hours later, not yet definitely in labor, she was given an ounce of castor oil followed by the same amount of quinine for four doses every half hour. Moderately severe labor pains followed at irregular intervals. When the cervix was 4 or 5 cm. dilated and the vertex at -1, the membranes were ruptured artificially but only a moderate amount of fluid exuded. She was now given a small dose of one of the barbiturates and one hour later delivered spontaneously a normal male infant weighing 8 pounds 13 ounces. Light open drop ether was administered for four minutes.

Immediately after the birth of the baby an enormous amount of amniotic fluid followed. This was then followed by a steady but moderate flow of blood. The

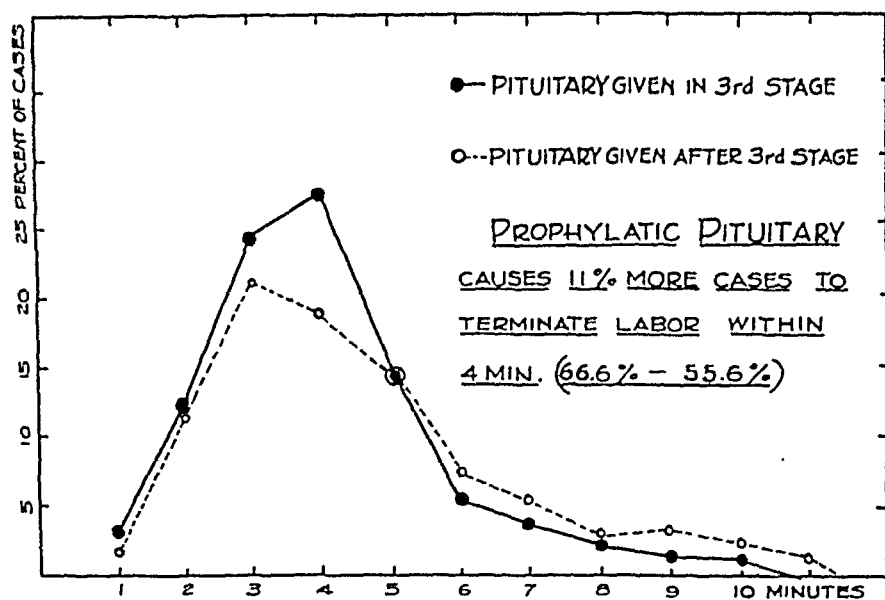


Fig. 4.—Length of the third stage.

placenta had separated and was expressed with the membranes one minute after the birth of the baby. One cubic centimeter of a solution of the posterior pituitary was given intramuscularly at this time. Bleeding continued and two minutes later 1 c.c. of a solution of ergot was given hypodermically. Three minutes later the blood loss totaled 800 c.c. and 1/320 of a grain of ergonovine was given intravenously. A 5 per cent solution of glucose was now started as the pulse was becoming rapid, although the general condition was not alarming. Because of continued bleeding, another ampoule of ergonovine was given in glucose solution, being administered intravenously. The birth canal and the uterine cavity were now quickly examined and a uterovaginal packing resorted to one-half hour after delivery when the blood loss totaled 1,400 c.c. Blood continued to ooze through the packing, and it was therefore removed and another packing inserted. The patient's condition was now critical. She died an hour and a half after delivery, as a blood transfusion was being given. An autopsy was not obtained. A careful postmortem examination of the generative tract revealed no lacerations or varicosities, and the uterine cavity contained numerous small walnut-sized clots. The total measured blood loss was 2,100 c.c. which represents 2.75 per cent of the patient's weight.

4. Prophylactic administration reduced the incidence of postpartum hemorrhage by 2.7 cases per thousand. It had no effect on the cause of hemorrhage, but did reduce the blood loss in hemorrhages due to atony by as much as 16.5 per cent. And inasmuch as the average postpartum hemorrhage with an atonic uterus amounted to 1,060 c.c., the saving was considerable.

5. The earlier administration of pituitary extract shortened the third stage of labor causing 11 per cent more patients to terminate this stage within four minutes. This helped to increase the number of cases in the group having the lowest blood loss.

6. If the placenta is delivered within five minutes, prophylactic injection does not lessen appreciably the blood loss. However where the third stage lasts between six and ten minutes, the blood loss is reduced 14 per cent, and where the placental stage requires more than ten minutes, the blood loss is reduced 7.5 per cent. But the average blood loss in these two groups is 250 and 380 c.c., respectively, and inasmuch as the percentage saved is inversely related to the amount of blood loss, the maximum saving does not amount to an ounce and a half.

7. The complications of the third stage are about equally distributed in both series.

CONCLUSION

The effective control of post-partum blood loss is the result of careful management of the third stage of labor based on a thorough knowledge of the physiology and pathology involved. The prophylactic administration of solutions of the pituitary body is not productive of more trouble, and appreciably reduces the blood loss in hemorrhages due to uterine atony only.

I am most grateful to Dr. L. D. Moorhead, Dean of Loyola University Medical School and President of the Board of Directors of the Lewis Memorial Maternity Hospital, and to Dr. Morgan J. O'Connell, the Obstetrician-in-Chief with whose permission I have conducted this study.

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series in which pituitary extract was administered following the expulsion of the placenta, but the difference is too small to be convincing.

In an effort to explain why the prophylactic injection of solutions of posterior pituitary does not frequently cause trouble, Calkins stated that "it requires from seven to ten minutes to produce a severely hard

TABLE V. COMPLICATIONS OF THE THIRD STAGE

	MANUAL REMOVAL OF THE PLACENTA			REMOVAL OF RETAINED COTYLEDONS	DILATATION AND CURETTAGE
	CASE	TIME	INDICATION		
Pituitary extract before	1	14 min.	Hemorrhage and hourglass contraction	5	1
	2	40 min.	Hemorrhage	Removed immediately	
	3	14 min.	Hemorrhage		
Pituitary extract after	1	2 hr.	Retention	3	2
	2	2 min.		Removed immediately	
		1 hr. 35 min.	Hemorrhage Hourglass contraction		

contraction of the uterus, and in a majority of instances the placenta will have been delivered before that time." The explanation does not appear adequate, because as shown in Fig. 4 it is clinically evident that pituitary extract acts in three to four minutes. Furthermore, kymographic tracings show that the first phase is a tetanic-like contraction which lasts several minutes, followed by waves of contraction and relaxation which are higher than the normal waves and decrease gradually in intensity.

Is it not probable that the hypersensitive uterus can be thrown into a state of disordered contraction by pituitary extract and thereby cause placental incarceration?

SUMMARY

The optimum time for the administration of pituitary extract in controlling postpartum bleeding is an unsettled question. A comparative study of the prophylactic administration in the third stage and administration after completion of the third stage is presented. The study involved 1,100 cases in each series and the results obtained are as follows:

1. The general average blood loss and the group percentage distribution are too nearly alike to concede an advantage to either method.
2. Investigation of induced and stimulated labors yielded inconsistent results.
3. There is a 5.5 per cent reduction of the blood loss in normal cases and a 6 per cent reduction of the average loss in operative cases when pituitary extract is administered prophylactically. The maximum saving is less than an ounce.

proper one and are following the custom of most writers, particularly the American obstetricians. Hence, we define an elderly primipara as that patient who has undertaken pregnancy in the latter years of the childbearing period, and in consequence one who has her baby between the ages of 35 and 45 years. A negligible number escaping this classification, due to the extreme of age, would, of the fact of their occurrence, constitute a problem all their own.

It can certainly be deduced by an inspection of the figures presented by different authors, notwithstanding a few of their more hopeful interpretations, that as far as toxemias, operative deliveries, morbidity and mortality rates are concerned most of the figures show beyond doubt the tremendously higher incidence of these complications in the elderly primiparae. We cannot pass without calling attention to the fact that many of the maternal deaths were postoperative after cesarean section. Von Khreninger-Guggenberger and Leutenmeyer caution against the use of cesarean section in elderly primiparae as being especially hazardous even with excellent indications, believing that these elderly primiparae do not stand the operation well, and in their thirteen operations they had four deaths.

Our cases are from the service of the Lying-In Hospital in New York where during the four-and-one-half-year period from Sept. 1, 1932, to March 31, 1937, there occurred on the indoor service 11,919 deliveries with the birth of 12,059 infants. Of this number there were 240 patients that fell into the elderly primiparae group, an incidence of 2.01 per cent. This figure agrees with that of most writers. It was found in most groups that the incidence is higher in private patients than in clinic groups. We have not made this distinction in the reporting of our material.

In our series, elderly primiparae showed an incidence of contracted pelvis of 15.5 per cent, differing not appreciably from that of the total clinic population, which is 14.4 per cent. However, on analysis of these contractions of the pelvis, they are in agreement with the statement frequently made that the major type of pelvic contraction in the elderly primiparae is of the funnel variety and is much higher than the incidence of this type in the younger primiparae.

In Table I we have attempted to list, so far as possible, the most significant complications of pregnancy and give their incidence in relation to the control series. The incidence is approximately the same in contracted pelvis and the occurrence of cardiac disease. In our series the incidence is greater in the case of the toxemias (almost 3 times), placenta previa (2 times), and myomata uteri, which is almost double the clinic figure. The high incidence of these complications may be extremely serious and may influence the ultimate prognosis in a given pregnancy. The incidence of a previous abdominal operation in

ELDERLY PRIMIPARAE*

A STUDY OF 240 CASES

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WE BELIEVE that an unprejudiced reporting of the results encountered in any obstetric problem will result eventually in an accumulated experience which will correct or substantiate impressions, too often erroneous, and if not settle that problem, will erect certain landmarks of significance that may be useful in its proper management. This paper is an endeavor to conform to this premise by attempting to evaluate the rôle of age as it affects the course of pregnancy and labor in that group of patients who present themselves for obstetric guidance with their first pregnancies at 35 years or older, to add our results to the few, but none the less significant, contributions that have preceded ours, and to which we have largely conformed in outline, in order that such observations and conclusions as we shall be able to offer can be more readily correlated and their value be more clearly deduced.

A review of the literature, which is characterized by the scant number of the American contributions in contrast to the large number from France, Germany, and the Scandinavian countries, indicates that there has not been accorded, in this country, this interesting and important subject the attention which it deserves. From the literature available the significant articles are not numerous; the majority of them dealing with such abstract angles of the subject as the economic, social, and other prevailing conditions, which have resulted in the large and ever increasing number of elderly primiparae; and spend little time with the actual personal study and analysis of such women and the reporting of observations that might assist in formulating an intelligent basis for prognosis and treatment in their care.

What constitutes an elderly primipara? The controversy on this point in the literature, to assign this term to any age group has proved as indefinite and unsatisfactory as have most attempts at medical classification. From limits as widely separated as 28 to 40 years denoting the upper limit of youth, we find that the majority of writers have established this boundary at 30 or 35 years. In accepting and following the dividing line as 35 years, we feel we have accepted the

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reference showing the seriousness of this complication is that given by Schultze who states that this one finding must be considered a definite danger signal. Supporting this, and it is typical of many, she cites the cases of unengaged heads in her series in which there were 36.8 per cent cesarean sections; and in addition there were 44.4 per cent dystocias noted in the remaining, only 11.1 per cent had easy labors; the fetal mortality was 27.7 per cent and the maternal mortality was 1.7 per cent in this group.

This one reference we considered of sufficient seriousness to justify any precautions that may be militated for the elderly primiparae and we believe it tends to substantiate our statement earlier in our remarks that the hazards associated with childbearing in the elderly primipara are of very certain existence. Certainly no one would have us believe that the figures given are in any measure comparable to a control series of young primiparae or a clinic control series of all ages. Does it not then follow that in any group where the operative incidence is so high, the results so uniformly poor, it is well to consider this group of patients a weighty obstetric problem in which one is more likely to meet more serious difficulty and the assumed risks are greater?

The incidence of different presentations in our elderly primiparae is approximately the same as in our control clinic series.

The shortest labor among the 240 elderly primiparae was 2 hours and the longest 102 hours. Compared to the control group, labor in elderly primiparae was definitely prolonged, i.e., 17.1 per cent compared to 11.2 per cent. Likewise in the elderly primiparae the second stage was prolonged over the clinic group, i.e., an incidence of 34.6 per cent compared to 18.0 per cent. Whatever may be the cause of this prolongation of labor in all its stages, be it rigidity of the perineum, rigidity of the cervix, poor uterine contractions, or congenital hypoplasia and a faulty isthmus, albeit the fact remains that this finding of prolonged labor is greater in the elderly primiparae, and its reflection in the course of labor and the type of delivery is all too apparent and many times the results appalling.

A significant and interesting set of figures appears in Table III, illustrating the type of delivery in our series contrasted with those of the control series. All operative procedures are higher in the elderly primiparae, i.e., 56.7 per cent instead of 25.1 per cent. Now many people claim that a high incidence of operative cases in elderly primiparae is not as serious or significant as in the younger patient, due to the fact that most of the operations consist simply of terminating the second stage prophylactically by low, or at best by midforceps. In order to refute this we turn to one of the best series published on elderly primiparae (Schultze) and find that in this group there were 35 patients assisted in the first stage; 28 manual dilatations; 4 cases

our elderly primiparae was 22.0 per cent. Some of these operations would conceivably not be carried out on younger individuals; but in the last analysis operations such as cervical amputations, myomectomies, ectopic pregnancies, and salpingectomies from all causes, as well as some types of uterine suspension, should be considered a distinct factor in trying to offer a prognosis to such a patient and due to her age might influence the handling of such a patient at term. The literature is full of cases so complicated from previous abdominal operations, and the outcome in such cases in a significant percentage has been unsatisfactory to both mother and child.

TABLE I. COMPLICATIONS OF PREGNANCY

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Contracted pelvis	15.5%	14.4%
Cardiac disease	3.7%	3.9%
Toxemia	22.5%	8.1%
Syphilis	0.4%	1.0%
Tuberculosis	1.2%	0.4%
Myoma uteri	8.3%	4.9%
Placenta previa	0.8%	0.5%
Pyelitis	2.5%	1.3%
Epilepsy	0.4%	0.1%

Table II shows the complications of labor, which we have listed in the manner of several other authors. We have compared these to our control series of the general clinic population. The greater incidence of occipitoposterior positions, arrested transverse positions, and postpartum hemorrhage is remarkable. Of great significance is the large

TABLE II. COMPLICATIONS OF LABOR

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Persistent occiput posterior	11.2%	8.4%
Floating head at term	53.3%	20.9%
Postpartum hemorrhage	8.7%	6.7%
Arrest in midforceps	7.1%	4.5%
Placenta previa	0.8%	0.5%
Prolonged labor	17.1%	11.2%
Prolonged second stage	34.6%	19.0%

percentage of elderly primiparae who come to term with the head of the child unengaged (53.3 per cent, in contrast to that in the control series 20.9 per cent). The operative incidence in this group of elderly primiparae (being only about half of the total elderly group) is 68.8 per cent and 41.9 per cent in the control group. To state it differently we may say that at term with the head floating the incidence of spontaneous delivery in the elderly primiparae is only 31.2 per cent compared to 58.1 per cent in the control group. The most significant

proper obstetric indications, and therefore an incidence of 12.9 per cent shows that there are certainly about three and one-half times more complications arising in elderly primiparae that demand cesarean section than in the ordinary clinic group. The figure of 12.9 per cent represents an irreducible minimum which is in marked contrast to the clinic figure of 3.6 per cent; and if to this we add other sections on an "elderly primiparae" indication we might find ourselves reporting a figure so high that of itself it would be incompatible with any known sound obstetric system.

The incidence of episiotomies was 67.9 per cent in contrast to 62.8 per cent in the control series. This figure is not as high as that given by most authors who hail this procedure as a boon to the elderly primiparae and report 80 to 90 per cent performance of this procedure. To us our figures show that as far as the perineum is concerned in vaginal deliveries, the contention of some that perineal rigidity is great, cannot be taken without reservation, and that there must be other and more serious factors, which we have tried to point out, to explain the high operative incidence with its subsequent reflection in the mortality and morbidity rates.

The weights of the infants of elderly primiparae do not vary essentially from the clinic group. In marked contradistinction to the opinion usually held that the children of elderly primiparae are generally of excessive size, it may be said that the largest series of such reported shows the weights of the babies born to women of this age group to be smaller by 240 gm.

TABLE V. CAUSES OF INFANTILE MORTALITY

Prolapsed cord	2
Toxemia of mother	6
Syphilis	2
Antepartum hemorrhage	2
Malformation	2
Intracranial hemorrhage	4
Contraction ring	1
Intrapartum infection	1
Cord about neck	1
Cause unknown	5
Gross infantile mortality	10.7%
Gross infantile mortality, total clinic population	4.1%

We present our figures on infantile mortality in Table V. By "infantile mortality" is meant all premature and full-term infants, dead-born, stillborn, or dying within fourteen days following birth. We report a gross infantile mortality of 10.7 per cent in contrast to 4.1 per cent in the control series. We find some of the reports to have corrected figures. We have given our figures as gross in order that they may be evaluated by those interested. The infantile mortality, as re-

of Dührssen's incision; and 3 cases of dilatation aided by the insertion of a bag. In most series the indications for interference are not given and, true, many may be as intimated above, but this we know: that in our series none of the operative deliveries were done on the indication

TABLE III. TYPE OF DELIVERY

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Spontaneous	43.3%	74.9%
Forceps (all types)	36.6%	14.9%
Cesarean section (all types)	12.9%	3.6%
Breech extraction	4.5%	4.4%
Version and extraction	1.6%	0.7%
Craniotomy	0.4%	0.1%

of prophylaxis or on the indication of elderly primipara per se, except for 2 cesarean sections. We adhered to the clinic standard, in all cases, for the operative indications applying to all patients, hence it may be said that the same complications necessitating the employment of operative methods in the termination of labor in the elderly primiparae are twice as high as that of the clinic control group.

TABLE IV. INDICATIONS FOR CESAREAN SECTIONS

TYPE	NO. OF CASES
Placenta previa	2
Premature separation	2
Disproportion (trial labor)	2
Disproportion (contracted pelvis)	6
Pelvis and spine deformity	1
Contracted pelvis and breech	1
Acute yellow atrophy	2
Disproportion (infection), Latzko	1
Myoma uteri obstructing inlet	4
Myoma uteri (transverse presentation)	1
Cervical dystocia	2
Preeclampsia	1
Contracted pelvis and cervical stenosis	1
Contracted pelvis and recent myomectomy	1
Chronic nephritis (sterilization)	1
Chronic nephritis	1
Myoma uteri and extreme funnel pelvis	1
Premature rupture of membranes with disproportion	1
Elderly primigravida	2

Several authors do not hesitate to fall back upon "elderly primiparae," as an indication for cesarean section. In our series all sections were done for pure obstetric indications, except the two cases previously referred to. It is one of the purposes of this study to determine whether or not broadening the indications for cesarean section in this group of patients would give better results than the indications we now rigidly adhere to. We believe that all the cesarean section operations in this group of elderly primiparae were performed on

SUMMARY

We have called attention to the widespread impression entertained by both the laity and the profession that elderly primiparae are more prone to the serious complications of labor and pregnancy and that in entering into this group the patient assumes a greater risk than her younger sister. We have attempted to show, by the use of our clinic material, that these apprehensions are in some measure well founded by actual obstetric experience and not "tradition" as it has been so often called. We have given available figures from the literature on many of the salient features of "elderly primiparae" which, in the main, have substantiated our conclusions that there is a marked increase in the incidence of toxemias, particularly the more serious types; that the operative incidence is at least double that of the ordinary clinic population; that the infantile mortality is markedly elevated; that the maternal mortality is four times greater than the clinic population; that labor is definitely prolonged and that morbidity and puerperal infection rates are significantly increased.

It is to be hoped that with the advances being made in obstetrics, particularly in the fields of endocrinology and x-ray pelvimetry, we may soon have at our disposal means of prognosticating more accurately in a given case the dangers that are to be avoided and so be more properly equipped to guide these patients through their pregnancies at a time when the value of a child is perhaps relatively greater. Premature induction of labor and the broadened indications for the employment of cesarean section operations do not, in the light of the figures studied, seem to clarify to any significant degree the manifold phases of the problem of elderly primiparity. By publishing the results of actual cases studied, uncorrected, and by making available to others whatever measures have served to improve the results in any given complication; together with what we may be able to gather from the advances now in progress, we may hope to bring about considerable improvement in both morbidity and mortality.

Until these methods are at our disposal, it is unwise to proceed on the assumption that elderly primiparae differ very little from the younger primiparae.

From our evidence presented, we are forced to conclude that an elderly primipara presents a distinct problem to the obstetrician and, consequently, that the teachings of some of the earlier writers to the effect that these women are more prone to the serious complications of gestation and parturition are well founded.

CONCLUSIONS

1. The incidence of elderly primiparae (35 years of age and over) is 2.01 per cent in a series of 11,919 obstetric patients.

ported by the various authors, is in general agreement with the figures we report. It is to be noted that there is no agreement in the literature as to what constitutes fetal mortality, certain authors reporting only full-term stillbirths, others deleting all cases where the fetal heart was not heard at the beginning of labor. It is for this reason that we advocate the term "infantile mortality," as defined above, because it reveals complete information as to the fate of the child.

Our maternal mortality, uncorrected, in the elderly primiparae, was 1.25 per cent in contrast to 0.2 per cent in the clinic control. The causes of death in the three cases were cardiac disease, questionable acute yellow atrophy, and peritonitis following cesarean section, respectively.

By "puerperal infection" is meant a rise in temperature to 100.4° F., or 38° C. which occurs once during each of two 24-hour periods following delivery or remains elevated longer than 24 hours, excluding the first 24 hours after delivery, unless the rise in temperature is definitely proved to be due to other causes, such as mastitis, pyelitis, or intercurrent infection. Morbidity includes all cases of puerperal infection and all those febrile from other causes. In this study we have observed a marked difference between the incidence of morbidity in the elderly primiparae and that in the clinic control group, the former being 21.6 per cent and the latter 11.4 per cent; while the incidence of puerperal infection is likewise elevated in the elderly primiparae to 12.5 per cent as compared to 8.6 per cent for the whole clinic.

There are other aspects of this problem about which it is difficult to obtain data but which are none the less important. One of the most important is that (discussed by Leopold Meyer) concerning the difference between the primiparae who married late in life and promptly conceived and those who married early and did not conceive until late. It is our impression, from the patients where this information was available, that in the latter group the complications mentioned in the total series of elderly primiparae are considerably more in evidence, i.e., the labor is somewhat longer; the operative incidence relatively higher; the toxemias occurred more frequently; and not the least important is that their labor was more likely to be of the weak unsatisfactory kind which we have come to speak of as desultory type. We believe their behavior in pregnancy and parturition is influenced by certain constitutional factors as well as some stigmata of genital hypoplasia, and these patients would probably not be ideal obstetric subject matter at any age. This group, however, forms only a small portion of our total series (2 to 5 per cent), and it is contended that here is only one, although perhaps the most important, of several factors involved.

PNEUMOCOCCUS INFECTION OF THE GENITAL TRACT IN WOMEN

ESPECIALLY DURING PREGNANCY AND THE PUERPERIUM

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AUFRECHT¹ demonstrated, in 1884, that the puerperal uterus of animals is a locus minoris resistentiae when pneumococci are injected into the blood stream. This finding was confirmed by Ortmann.² Weichselbaum,³ in 1888, found pneumococci in the endometrium and small uterine vessels in a case of fatal abortion during the course of a lobar pneumonia. Despite these and similar findings, American obstetricians and gynecologists have, if the literature is a criterion, shown but little interest in the subject of pneumococcal genital infections. The study of pneumococcal peritonitis and the allied genital infections has been carried on predominantly by pediatricians and surgeons.

These uncommon infections deserve more study than they have generally received not only because of their relation to occasional post-partum gynecologic manifestations in these patients, but also because they are so frequently expressions of an endogenous type of puerperal infection. They thus serve to remind us that endogenous infections do occur, and that organisms other than the streptococcus cause puerperal sepsis.

In this hospital three cases of pneumococcal puerperal infection have been identified during the six-year period from 1931 to 1936 inclusive. During this period there have been 20,364 deliveries in the hospital and outpatient department. All of these cases of infection of the genital tract have been secondary to pulmonary involvement. To be sure, other instances of pneumococcal pneumonia during the period of gestation and the puerperium have occurred during this period, some of which were fatal, but in only these three cases has the genital tract been shown to be involved in the disease process.

CASE 1.—(M. M. UH 10084.) The patient, a twenty-four-year-old white tertigravida, secundipara, between thirty-seven and thirty-eight weeks pregnant, was admitted Feb. 9, 1933, with a history of ruptured membranes of forty-eight hours' duration. Except for known latent syphilis the past medical history was not significant. Physical examination was negative. The pelvic measurements were consistent with a generally contracted pelvis. Labor was allowed to progress until the sixtieth hour when the patient was delivered by a low transverse cervical

2. There is an increased incidence, among elderly primiparae, of toxemia of pregnancy, placenta previa, and myoma uteri.

3. Although there is no marked difference in the total incidence of all types of contracted pelves in this group of women, funnel pelves are definitely more predominant than among younger primiparae.

4. Among the complications of labor in elderly primiparae, we note an increased incidence of occipitoposterior positions, arrested transverse positions, and postpartum hemorrhage. We also observe that the head of the child is unengaged at term in 53.3 per cent of elderly primiparae, as compared with a figure of only 20.9 per cent in a control series of patients.

5. The operative delivery incidence is greatly increased in the elderly primiparae, being double that of the clinic population.

6. Maternal mortality is definitely higher in the elderly primiparae group, than in the total clinic group of patients.

7. Infantile mortality, which includes premature, full-term and neonatal deaths, is markedly elevated in elderly primiparae, being almost three times that of the clinic population.

8. The elderly primipara does not seem to be able to undergo operative procedures at delivery with as good results to herself, as does the younger woman as shown by the complications of the puerperium.

9. "Elderly primipara," per se, does not constitute an indication for cesarean section, unless there is an accompanying complication, which still further adds to the risk to the offspring.

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Carcinoma of the female urethra now is being encountered and recognized much more frequently than formerly. It may appear in the third but usually occurs in the fifth decade of life. A positive Wassermann reaction may be present and so mar one's best efforts in arriving at an early diagnosis. A single biopsy specimen may be misleading. In spite of a report "no malignant condition found" the patient should be carefully watched and, when healing is unduly delayed, further sections obtained. One fourth of the patients in the author's series of seventeen had had "growths" removed from the urethra previously, a predisposing factor to malignant changes. Early recognition and properly instituted treatment give an appreciable measure of palliation. A four-year cure and probably longer may be expected in more than 50 per cent of the cases.

J. P. GREENHILL.

the same type of pneumococcus, in the tissue over the right ninth rib in the mid-axillary line. She convalesced uneventfully and was discharged well.

The placenta of this patient was most interesting as it showed a localized area of premature separation, with an associated septic ischemic infarct. In Giemsa and Gram stained sections through this area many Gram-positive diplococci, some of which were encapsulated, could be seen invading the infarcted area. The same organisms were found also in the maternal blood and fibrin along the decidual plate.

CASE 3.—(E. J. UH 3516.) The patient, a twenty-seven-year-old quadrigravida, tertipara, approximately thirty-two weeks pregnant was admitted Jan. 28, 1936, complaining of chills, fever, and a productive cough. Her obstetric and medical histories were negative until two days prior to admission when she experienced headache and general malaise. Twelve hours prior to admission she had a sudden chill, pain in the left chest, fever, and cough. On admission the temperature was 104° F., the pulse 120, the respirations 40. Physical examination revealed some râles and suggestive bronchial breath sounds at the left base posteriorly. The following day there were definite signs of lobar pneumonia involving the left lower lobe. The sputum was typed and a Type II pneumococcus found. 200,000 units of combined Type I and II pneumococcus antiserum (Fulton) were given intravenously in divided doses and the patient seemed definitely improved. That evening she spontaneously delivered a premature 3 pound, 4 ounce female infant by the breech mechanism. The baby was in poor condition from birth and subsequently died in the premature nursery. The next day the patient's temperature rose slightly and she appeared definitely more sick. Prognosis at this time was guarded. The admission blood culture contained Type II pneumococci and further serum was administered. On the fourth postpartum day the temperature was 103.8° F., the pulse 125, the respirations 38. The patient's general condition was poor. She had now received a total of 400,000 units of the combined serum. Blood cultures following the last serum treatment were repeatedly negative. Consolidation had spread, however, to involve the upper left lobe. The patient had foul lochia. Culture of the endocervix and lochia at this time yielded an almost pure culture of Type II pneumococci. An obstructing cervical plug was removed when the culture was taken. This improved uterine drainage. Simultaneously the patient began to improve steadily. Four days later the temperature was ranging between 98° and 99.5° F., the pulse was steady at 90. At this time there was noted some fluid in the left pleural space but repeated x-ray studies showed it to be resorbing and soon it had completely disappeared. The cervical cultures now proved negative, and on the twenty-eighth postpartum day the patient was discharged well. The placenta was carefully examined in this case but no evidence of any pneumococcal inflammatory process could be found.

The first of these cases demonstrated genital involvement in a widespread pneumococcal process. The organisms were not typed. The second case was shown bacteriologically to have identical type pneumococci in the sputum, blood stream, and pleural effusion. Associated with this was the finding of morphologically typical pneumococci in the placental infarct and in the maternal blood and fibrin along the decidual plate of the placenta. This lesion may illustrate the mechanism whereby the uterine wall is infected during a bacteremia. The third of these cases was shown bacteriologically to have similar type

cesarean section, because of combined cervical and pelvic dystocia. The infant weighed 5 pounds, 7½ ounces, and was in good condition. There was a moderate postoperative reaction, the temperature ranged from 99° to 100° F., the pulse was 120. On the fourth postoperative day the patient had a productive cough. The sputum was thick and greenish. Temperature 101° F., pulse 120, respirations 30. The clinical course was variable for two days, the cough became less productive, temperature 98.8° F., pulse 120. (At this time the infant was transferred to the Eye and Ear Infirmary with ophthalmia neonatorum.) On the ninth postoperative day x-ray study revealed a "typical lobar pneumonia" of the right upper lobe, but the temperature remained normal and the pulse was 100. On the fifteenth postoperative day the temperature, pulse, and respirations were rising and examination revealed an extension of the pneumonic process to the right lower lobe. On the twenty-first day the patient developed a septic arthritis of the right shoulder and elbow joints, which were swollen, hot, and very painful. The temperature, pulse, and respirations again rose sharply. From this time the patient's course was generally downhill, the temperature rose to 106° F., the pulse to 140. The patient became comatose and died on the twenty-ninth postoperative day.

In brief, the necropsy findings were: lobar pneumonia, involving the entire right lung; pneumococcemia; acute vegetative endocarditis—pneumococcal; pneumococcal meningitis; thromboses of the superior vena cava, right jugular, subclavian, axillary and brachial veins and the uterovesical venous plexus. Pneumococci, which were not typed, were recovered from the lungs, tricuspid vegetations (where they were associated on smear with some gram-negative diplococci), meninges, uterus, and various thrombi. Unfortunately no note was made of an examination of the inflamed joints. While a concomitant gonococcal bacteremia cannot be ruled out, the principal pathogen seems clearly to have been the pneumococcus.

CASE 2.—(E. G. UH 11160.) The patient, a twenty-nine-year-old secundigravida, primipara, approximately thirty-eight weeks pregnant, was admitted Dec. 30, 1935, with a history of a cold of two weeks' duration culminating in malaise, sudden chill, fever, pain in the chest, and dyspnea. Her previous obstetric and medical histories were essentially negative. On admission the temperature was 101° F., the pulse 120, the respirations 28. Physical examination confirmed the diagnosis of lobar pneumonia involving the left lower lobe. The following morning sputum typing revealed Type I pneumococci and serum therapy was instituted. During the day 110,000 units of combined Types I and II pneumococcus antiserum (Felton) was administered intravenously. The blood culture taken on admission revealed a Type I pneumococcus. The patient seemed clinically improved but serum therapy was continued because of the positive blood culture. On the fourth hospital day the second blood culture, taken before the administration of the last serum, also proved positive for pneumococci. At this time the patient's antibody titer, as determined by Dr. Finland of the Boston City Hospital, was found to be high. On the fifth day following admission more serum was given as the blood culture was again positive. Six days after the onset of her illness the patient spontaneously went into labor and delivered a full-term normal male infant. Up to this time she had received slightly more than 400,000 units of the combined serum. Clinically she seemed improved but physical examination suggested encapsulated fluid at the left base and a thoracentesis was done. Typical greenish yellow creamy pus was obtained which on culture yielded a pure growth of Type I pneumococcus. Following this the patient's course was irregularly febrile and on the sixth postpartum day she was transferred to the Massachusetts General Hospital for drainage of the empyema. There her subsequent course was uneventful except that following drainage of the empyema on the left she developed a subcutaneous abscess, due to

CASES FROM LITERATURE

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
<i>"Puerperal Infections,"</i>				
Apert ⁷	Peritonitis in puerperium associated with empyema	Pleural pus	R	
Armitage ⁸	Abdominal pain, normal delivery, lungs clear	Peritoneal pus	D	
Buettjer ⁹	6 wk. pp. developed salpingitis and pelveo-peritonitis, later lobar pneumonia with bacteremia	Peritoneal pus Blood	R	Type II
Idem	5 wk. pp. developed sudden peritonitis, lungs clear until terminal pneumonia	Peritoneal pus	D	
Idem	Multip. 8 mo. pregnant developed peritonitis	Peritoneal pus	NS	
Bondy ¹⁰	Normal delivery, manual extract. of secundines, peritonitis, lungs clear	Lochia	D	
Brawerman ¹¹	Spont. delivery, sepsis with endometritis, endocarditis and meningitis	Endometrium Endocardium Meninges	D	
Bumm ¹²	Lobar pneumonia in puerperium, peritonitis	Lochia	D	
Burchhardt ¹³	Lobar pneumonia, spont. delivery	Uterine vessels Placental site	D	Pneumoc. in shoulder joint in life
Idem	Spont. delivery, sepsis with meningitis on second pp. day	Uterine lymphatics Endometrium	D	
Canon ¹⁴	Normal delivery, sepsis, death on twenty-first pp. day	Meninges Thyroid abscess Ovarian abscess Blood (PM)	D	
Czenetschka ¹⁵	Lobar pneumonia, normal delivery	Meninges Endocardium Uterine lymphatics Peritoneal pus	D	Infant died of pneumonia
Darre, Laederich and Mamout ¹⁶	Normal puerperium until onset of peritonitis	Peritoneal pus	R	
de la Marniere ¹⁷	Gastric distress antepartum, normal delivery, peritonitis later assoc. with suppuration of dermoid cyst		R	
Feulerton and Bonney ¹⁸	Forceps delivery, sepsis		D	
Idem	Pneumonia, premat. delivery at 7½ mo., death	Lochia Blood, lungs, spleen, uterus	D	

*R. recovered; D. died; NS, not stated.

pneumococci in the sputum, blood stream, and lochia. This was a case of true pneumococcal endometritis. It is of some interest, also, to note that all three cases occurred during the winter season.

REVIEW OF LITERATURE

Reports of pneumococcal puerperal infections have appeared almost entirely in the foreign literature, with but occasional reports originating in this country. The following cases have been found in a study of this literature and, with the exception of those noted as quotations from Bondy^{11, 12} and two abstracts,^{26, 34} have been verified by reference to the original articles. The classification of these cases, based on these reports, is of necessity a loose one. There is some overlapping in the groups and one group is included only because of the valuable comparison it offers. "Puerperal infections" include some instances in which no definite genital involvement was proved but was assumed as no other source of infection was found. Similarly "peritonitis in pregnancy—undelivered" includes three cases without definite genital involvement, but is closely allied to the puerperal infections and consequently of interest to obstetricians and gynecologists. The division "infection associated with abortion" is included as a separate entity in order to compare those infections occurring early in pregnancy with those occurring in the last trimester. To further complete the review and furnish a worthwhile contrast to the more generalized infections a group of "localized abscesses" is included. No attempt has been made to review pneumococcal peritonitis in general, though many of these cases, e.g., those of Lambert,⁴ Gibson⁵ and Peck⁶ are of interest in any discussion of the source of these genital infections.

Whence comes this infection of the generative tract? This has been a subject of contention almost since the first cases were reported. Many of these patients were presented by their authors as having had a primary infection ascending through the generative tract, in contrast to a secondary or hematogenous infection. In many of the so-called primary cases the validity of such an assumption is subject to doubt due to incomplete examination, and in none was the source definitely proved. The remaining cases have been presented as complications of a pneumococcal process elsewhere in the body, or in the absence of any history as examples of an interesting uncommon lesion.

The earlier authors believed that either primary (ascending) or secondary (hematogenous) infections could occur but emphasized that a primary source could be assumed only after every possible older focus was eliminated by thorough clinical, pathologic, and bacteriologic studies. The lungs and heart were held by Bondy¹⁰ and Hornung³⁹ to be the two major primary foci that were to be eliminated. This attitude practically demanded a complete autopsy study before assuming a primary source. Lord and Nye⁵³ in studying the pneumococcus found it could not long survive at the pH of the normal vagina, which as shown by various authors and

CASES FROM LITERATURE—CONT'D

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
<i>"Peritonitis in Pregnancy" (Undelivered)</i>				
Elkin ³³	7 mo. pregnant, lobar pneumonia, peritonitis	Sputum, blood	D	
Federici ³⁴	6 mo. pregnant, peritonitis. Heart and lungs clear	Peritoneal pus Blood and urine	D	
Harteman and Lacourt ³⁵	Bilat. lobar pneumonia, peritonitis	Lungs Peritoneal pus	D	Fetus also had pneumonia
<i>"Infections Associated With Abortion"</i>				
Reuly ¹⁰	Abortion, sepsis associated with old endocarditis	Blood	D	
Cohn ³⁶	3 mo. postabortion, metritis, meningitis. At post: retained placenta. Lungs clear	Uterus Meninges, spinal fluid, endocardium, endometrium	D	
Federici ³⁴	Abortion, bacteremia, associated with pleuritis	Blood	D	
Fox and Bordoni-Uffreduzzi ³⁷	Lobar pneumonia, abortion at fourth month	Uterus Uterine veins	D	
Idem	Lobar pneumonia, abortion at sixth month	Fetus Uterine veins	D	
Foulerton and Bonney ¹⁰	Incomplete septic abortion at 3 mo. Lungs clear	Fetus Lochia	R	
Fricke ³⁸	Abortion, bacteremia and peritonism	Blood	R	Serum therapy
Hornung ³⁹	Induced abortion, sepsis, meningitis, lungs clear	Blood, spinal fluid, lochia	D	
Idem	Induced abortion, sepsis with cardiac signs	Blood (life)	D	Uterus not examined
Idem	3 mo. pregnant, incomplete abortion, meningitis	Spinal fluid, blood and lochia	D	
Jensen ⁴⁰	3 mo. pregnant, abortion. No history of pulmonary involvement	Peritoneal pus	D	Mixed with <i>B. proteus</i>
Stravoskiadis ³⁰	6 mo. pregnant, lobar pneumonia, endometritis	Lungs Endometrium	D	
Idem	4 days postabortion devel. meningitis. Pneumonia	Lungs Endometrium	D	
Vlach ⁴¹	Abortion, D. & C., sepsis, terminal pneumonia	Blood (life) Meninges	D	Mixed with staph.
Weichselbaum ³	Pleuritis, abortion	Pleural pus Endometrium Uterine vessels	D	

CKOIS-HERTIG : PNEUMOCOCCUS

CASES FROM LITERATURE—CONT'D			PNEUMOCOCCUS IN—		REMARKS
AUTHOR	CLINICAL COURSE IN BRIEF	LOCATIONS	OUTCOME		
Idem ¹⁹	Term delivery, sepsis	Lochia	D	Associated with <i>B. coli</i>	
Idem	Term delivery, retained membranes	Placental site	R	Mother not posted	
Laffont, Castanier and Lavallo ²⁰	Term delivery, eclampsoid symptoms due to meningitis	Vagina	D	A rare case	
Laffont and Ezes ²¹	"Cold," normal delivery, sepsis, pelvic phlebitis	Infant	D	Infant died at forty-ninth hour	
Levy ²²	Pneumonia, premat. delivery at ninth mo.	Pelvic veins	D		
Lop ²³	Normal delivery, douche, sepsis, lungs clear	Pleural pus (mother)	R		
McCord ²⁴	Normal delivery, peritonitis on third pp.	Blood and lungs of infant	D		
Idem	Normal delivery, sepsis, lungs clear	Lochia	D		
Monckeberg ²⁵	Op. delivery, endometritis, pneumonia later	Peritoneal pus	D	Pneumoc. in throat of midwife	
Pruska ²⁶	Op. delivery, meningitis, lungs clear	Peritoneal pus	D		
Idem	Manual removal of placenta, endometritis, pleurisy	Blood, lochia	D		
Schuhl ²⁷	Low forceps, peritonitis, lungs clear	Lochia (second day)	D		
Seymour ²⁸	Bacteremia on fourth pp. day, lungs clear	Lungs and uterus	D		
Smith and Spriggs ²⁹	Breech extr. with craniotomy, endometritis	Meninges	NS	Primary source assumed	
Stravoskiadis ³⁰	Developed pneumonia on first pp. day	Uterus	R	Uterus not examined	
Idem	Pneumonia, spont. delivery, peritonitis, operation, death	Lochia	D	No definite uterine involvement, infant infected	
Wetzel ³¹	Puerperal endometritis	Lochia	D		
Zangemeister ³²			NS		

most recently by Oberst and Plass,⁵⁴ varies between 4.0 and 5.0. Shutt⁵⁵ working on the problem of wound infection by pneumococci substantiated this and concluded therefore that pneumococci could not enter the uterus as an ascending infection. But it has been shown by various workers^{54, 56, 57} that the vaginal pH varies widely, apparently as a result of a disturbance of the normal symbiosis of the vagina and microorganisms of the group *B. acidophilus*. Injury to the vaginal wall, massive contamination and dilution and constitutional weakness are several of the factors which may disturb this symbiosis. Chronically ill and debilitated patients tend to have an alkaline reaction. Abraham⁵⁸ has shown this also to be true for children, thus confirming McCartney's⁵⁹ observation of the correlation of alkaline vaginal reaction in children with pneumococcal peritonitis. Similarly it has been shown^{54, 56, 57} that the complexity of the vaginal flora increases directly as the pH rises. On this basis we must admit that a primary genital infection is possible, more especially in the parturient than the pregnant patient, if vaginal acidity is the defensive mechanism it has been assumed to be. King⁴⁶ basing his arguments primarily on the work of McCartney believes the primary source is the common one.

That this is so is most questionable in view of the many foci of pneumococci in the apparently normal person, notably the middle ear and nasopharynx. That a bacteremia or meningitis can follow spread of the organism from these foci without the intervention of a pulmonary infection is now accepted as fact. This is the explanation given in the cases of so-called "primary" peritonitis in the male. In all probability some of the cases reviewed in which a meningitis occurred were cases of this kind. An interesting case illustrating this process is the following:

CASE 4.—(L. McK. UH 12877.) The patient, a twenty-eight-year-old white sex-tipara delivered spontaneously, at home, a normal 8 pound, 4 ounce infant. When seen by a physician approximately one-half hour later, the placenta was still adherent and could not be expressed by gentle Credé method. The patient had bled nearly 1,000 c.c. and was in beginning shock. She was given emergency shock treatment and transferred to the hospital, where, on admission Jan. 22, 1934, the blood pressure was 60/0, the pulse thready and rapid, the skin cold and moist. As soon as possible she was transfused with compatible blood. The clinical improvement was rapid, therefore the patient was prepared and the placenta removed manually. Further improvement was aided by a second transfusion while the patient was still in the operating room. On the fourth postpartum day the patient had a sudden chill, the temperature rose to 103.4° F., there were a few coarse râles at the left base posteriorly, and the patient had a slight cough. This condition was but transient and the next day the temperature had returned to normal and cough disappeared. Her course was afebrile for five days and on the ninth postpartum day she was allowed to sit up. On that day she had a vaginal douche. The next day the patient got up but soon returned to bed complaining of general malaise and a headache. Shortly after this she had a sudden chill. The temperature rose to 104° F., the pulse to 140, accompanied by marked nausea and vomiting. Physical examination at this time was reported as negative. Two hours later she had a generalized convulsion which began in the upper extremities. Six hours later there was beginning rigidity of the neck and Kernig's sign became positive. Spinal puncture was done and 40 c.c. of antimeningococcic serum was given intravenously.

CASES FROM LITERATURE—CONT'D

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
Wolfsohn ⁴²	3 days postabortion peritonitis, lungs clear	Peritoneal pus	D	
Idem	20 days postabortion, peritonitis	Lochia and uterus Peritoneal pus	R	
	"Localized Abscesses" (Tubal, Ovarian and Pelvic)			
Bondy ¹⁰	No history	Pyosalpinx	NS	
Idem	No history	Pyosalpinx	NS	
Canon ¹⁴	Assoc. with uterine Ca.	Pyosalpinx	D	
Cole ⁴³	Lobar pneumonia, pelvic abscess	Peritoneal pus	R	
		Sputum		
		Pus from pelvis		
Fricke ³⁸	No history	Pyosalpinges-bilateral	NS	
Frommel ⁴⁴	Last puerperium febrile after op. delivery	Pyosalpinx	D	Patient had apical tuberculosis
Gibson ⁵	Pelvic symptoms for 2 years. Incision and drainage	Pus	R	
Hartmann and Morax ⁴⁵	No history	Pyosalpinx	NS	
Idem	No history	Pyosalpinx	NS	
King ⁴⁶	No pulmonary involvement	Tuboovarian abscess	R	
Idem	"Flu" prior to admission	Pelvic abscess	NS	Type IV
Idem	"Cold" associated with present illness	Pelvic abscess	NS	Type IV
Pearce ⁴⁷	No history	Pyosalpinx	D	
		Peritoneal pus		
Ploeger ⁴⁸	No history	Pyosalpinges-bilateral	D	
Idem	No history	Pyosalpinges-bilateral	D	
Idem	Uterine Ca. with associated pelvoperitonitis	Pyosalpinx	D	
von Rosthorn ⁴⁹	Febrile puerperium, 6 years of abdominal symptoms. No pulmonary history	Pelvic pus	R	
		Pyosalpinx		
Tompkins ⁵⁰	No history of pulmonary involvement	Pelvic abscess	R	Type I
Idem	No history of pulmonary involvement	Tuboovarian abscess	R	Type IV
Idem	Past history of pneumonia	Tuboovarian abscess	R	Type III
Witte ⁵¹	Normal delivery 5 years previously, lungs clear	Tuboovarian abscess	R	
Wolfsohn ⁴²	Pulmonary tuberculosis	Pelvic abscess	R	
Zweifel ⁵²	No history of old focus	Tubal masses	R	

of exposure, whether it is the increased general resistance and good health due to adequate medical supervision, whether there is some possible specific immunity inherent in the pregnant state, or a combination of these factors, that is responsible for this lower incidence, is not known. Tompkins⁵⁰ statement that saliva is a potentially dangerous lubricant for condoms implies that the ascending route must at all times be a negligible one as undoubtedly this is the most common of the lubricants, especially among the poorer classes. No particular prophylactic measures during labor and the puerperium are indicated other than the usual careful treatment of the patient.

The treatment of a generalized pneumococcal infection, including peritonitis, should be a conservative one with the addition where possible of specific antisera. The treatment of the localized lesion is surgical drainage.

SUMMARY AND CONCLUSIONS

Three cases of pneumococcal puerperal infection have been presented. The pertinent literature has been reviewed and the abstracted cases tabulated. All three of our own cases were endogenous in type. While many of the cases reviewed were thought to be of exogenous origin, none can be definitely proved so and an endogenous source appears more probable in most. That the exclusion of an endogenous source requires very complete clinical and laboratory studies is illustrated by a reported case of nonpuerperal pneumococcal infection.

The incidence of known pneumococcal puerperal infection in this hospital is one in 6,788 deliveries. It has been pointed out that this incidence is probably low due to the failure to identify organisms loosely classed as "nonhemolytic" or "green" streptococci. The prognosis in the localized infection has been shown to be much better than in the diffuse process. Treatment appears to be greatly aided if a specific antiserum is available.

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when the spinal fluid was found to be turbid though under normal pressure. Study showed this fluid contained 2,500 W.B.C. per c.mm. and many Gram-positive diplococci, which on culture proved to be pneumococci. The patient's course was constantly downgrade, and she died twenty-eight hours after the onset of the initial chill. Clinically the sequence of events was believed to be: pelvic phlebitis, pulmonary embolus, and septic meningeal embolus from the lung.

At necropsy the lungs and heart were found negative throughout, as was the genital tract. There were found an acute tracheolaryngitis, a pneumococcemia and a pneumococcal meningitis. Postmortem cultures of the meninges and blood were positive for the pneumococcus, the antemortem blood culture remained sterile. In the absence of so complete an examination, this case might well have been assumed to be of primary genital source, especially with the history of manual removal of the placenta. Search for a pneumococcal focus in either the pelvis or lungs was, however, unavailing. The acute tracheolaryngitis seems the probable source of the organisms causing the meningitis.

Study of these cases of pneumococcus infection in the future may, with typing of the organism, be much more clearly defined as to source. For the present we must agree with Bondy and Hornung that either type of infection is possible but the assumption of a primary source is permissible only after exhaustive study—clinical, bacteriologic, and pathologic.

Twenty-three pneumococcal infections of all types occurred during the period under study. This is an incidence of 1 in 855 deliveries. Of these three, or 1 in 6,788 deliveries, had a pneumococcal genital infection. It seems probable that this incidence is low and that more careful bacteriologic studies will differentiate more true pneumococcal infections from that heterogenous group of infections attributed to *Streptococcus viridans* or "nonhemolytic" streptococcus.

From a statistical summary of the reviewed cases we can learn something of the prognosis:

	RECOVERED	NOT STATED	DIED
37 Puerperal infections	9-24.3%	3-8.1%	25- 67.6%
3 Peritonitis in pregnancy			3-100.0%
17 Infections associated with abortion	3-17.7%		14- 82.3%
57 Total diffuse infections	12-21.0%	3-5.3%	42- 73.7%
23 Localized abscesses	11-48.0%	6-26.0%	6- 26.0%

While these figures, obviously, are not to be taken as showing any more than a trend they do show the marked difference between diffuse and localized infections. Our own cases suggest that the prognosis in cases treatable by a specific serum appears definitely improved.

Prophylaxis is, of course, the major consideration in a discussion of the treatment of these conditions. General antenatal care seems the best prophylactic measure. The incidence of pneumococcal infection is said to be lower in pregnant women than in the general population. Whether it is the dislike of meeting strangers while large with child and the resultant avoidance of crowds, thus decreasing the probability

blood CO_2 evidence of alkalosis. Moreover, chloride contents had not been lost during postoperative vomiting which is recognized as a factor in this alkali acid imbalance.

Patients evidencing mild shock to extreme collapse at the time of delivery have been observed innumerable times. Quite often it has been encountered very shortly after the beginning of the anesthetic, but more often accompanying the necessary deep anesthesia for the termination of dystocias. Past judgment has always labeled such tragic complications as cardiac failure, pulmonary embolus, surgical shock and if death ensued, postanesthetic deaths. Recent observation and studies upon such patients long in labor have revealed occasionally the presence of acetone and diacetic acid in the urine, while the blood CO_2 estimation almost consistently showed the presence of severe acidosis.

An interview with a supervising nurse of an obstetric service even before this study was begun disclosed the possible cause for the presence of acetone and diacetic acid in the urine. She remarked "that the anesthetist requested fluids to be limited at least during the second stage of labor, so as to avoid the vomiting associated with anesthesia." Further inquiry revealed that many patients received very little food due to the discomforts of labor and analgesia. The forcing of fluids and the giving of food has eliminated this type of acidosis. Therefore, it was assumed to be a mild starvation and dehydration acidosis resulting from the limitation of fluids and food. The giving of glucose intravenously as a prophylactic in all cases in labor over thirty hours before an anesthetic or obstetric operation is started has also played an important part in bringing about such gratifying results.

Further blood studies of patients dying after long and difficult labors showed the presence of a marked acidosis which failed to respond to the usual combative measures, i.e., glucose and insulin. This inclined us to believe that either of the extreme alternations in alkali acid ratio may be reached before death and that this is a primary or important contributory factor, which if recognized or corrected may reduce the unfavorable results. It so happened during our routine blood CO_2 estimation of normal labor, that a patient was admitted after having been in labor for five days. She was in extreme shock with low blood pressure and a rapid pulse. The skin was cold and clammy. The blood CO_2 was 15 volumes per cent. The urine showed no acetone and diacetic acid. This has been a frequent finding in extreme labor acidosis. Glucose and insulin were administered with no response such as had been noted in previous cases. As a result of this experience, we decided to conduct a clinical experiment with the hope that this patient's condition could be more effectively combated. One of us suggested sodium bicarbonate solution intravenously, as this has been used successfully in controlling the severe acidosis of uremia. Accordingly, a 2 per cent solution of sterile sodium bicarbonate was given and the blood CO_2 estimations recorded. There was a distinct CO_2 elevation and the patient's general reaction was favorable, and it

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AN EXPERIMENTAL STUDY OF ACIDOSIS AND ALKALOSIS IN LABOR*

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THE necessity of the normal alkali maintenance for health has been clinically appreciated for many years. Formerly, a patient free of organic disease was assumed to be a sound subject for any gynecologic or obstetric procedure. The physiologic approach to analysis of sudden unaccountable deaths has revealed that many were due to marked disturbances in the blood alkali acid ratio. Several years ago one of us encountered a severe alkalosis in a patient thought physically fit following a prolonged anesthetic for a simple gynoplastic procedure. The patient failed to respond to the available therapeutic measures, i.e., hypertonic salt solutions and blood transfusions. More recently a second patient received a prolonged gas anesthetic for an operation on a rather extensive pelvic inflammatory condition. Several hours after operation, she went into shock associated with complete anuria. The anuria was intermittently overcome by the introduction of glucose solution, but to our astonishment the carbon dioxide estimation revealed a fairly marked alkalosis of 78 instead of an acidosis as anticipated. In other words, both of these patients, in excellent condition, had received a prolonged gas anesthetic and presented the

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presence of acetone and diacetic acid. There was a constant lowering of the blood CO_2 as labor progressed, which reached the lowest point at the end of the second stage with recovery to normal immediately following delivery. This is in accord with most observations. The interesting fact was that the degree of acidosis was always in direct ratio to the hours and character of labor. This increasing acidosis was assumed to be the accumulation of lactic acid resulting from increased muscular activities. While we recognize the desirability of estimating the normal lactic acid content during labor, this was beyond the scope of our department which is essentially clinical with very limited biochemical facilities.

Table I presents the blood CO_2 estimations done in 157 patients during the first stage of labor. The lowest was 21.6 vol. per cent, the highest 56 vol. per cent. The average reading for the 157 patients was 42.98 vol. per cent. This indicates a moderate acidosis for the average, but the ones of interest are those with extremely lower readings who in some instances unless combated would pass over to a pathologic state. Therefore, it is advisable to keep in mind the possibility of such patients with a tendency towards the greater degrees of acidosis.

EXPERIMENT 1. ACIDOSIS PRODUCED BY ETHER ANESTHESIA

DOG	CONTROL	DURATION OF ANESTHESIA	2ND CO_2	DECREASE	INCREASE	CONDITION OF DOG
6	50 Vol. %	20 min.	42%	8 Vol.	3 Vol.	Normal
7	57 Vol. %	20 Min.	48%	9 Vol.		Starved 3 days
8	46 Vol. %	35 Min.	35%	11 Vol.		Starved 3 days
9	52 Vol. %	30 Min.	55%			Moderate starvation
10	None	20 Min.	38%			Normal
10	38 Vol. %	45 Min.	31%	7 Vol.		Good
11	45 Vol. %	20 Min.	42%	3 Vol.		Good

The anesthetic was not carried to the end point, but there is a decrease in the blood CO_2 in proportion to duration of the anesthetic. There is an average decrease of 7.3 vol. per cent for the ether anesthesia of twenty-five minutes. This verifies the previous statement that anesthesia produces and intensifies the acidosis.

Table II includes the blood CO_2 estimations of 65 patients done during the second stage of labor, the average 40.05, lowest 29 and highest, 53.30. These observations substantiate the previously made statement that the acidosis increases as labor progresses and is intensified by the character of labor. The longer and more difficult the labor the greater the acidosis.

Table III includes 50 patients immediately after delivery. The average was 48.9, lowest 29.2 and highest 86.6. This observation records the immediate response of the blood CO_2 to normal after the cessation of muscular activity.

Feeling that the presence of diacetic acid and acetone in the urine due to dehydration and starvation and the acidosis evidenced by blood CO_2 was in direct ratio to muscular activity, it was decided to see the effect of various sedatives.

A study of sodium amytal in eight cases showed this drug had apparently very little effect upon the blood CO_2 . Three cases showed an average increase of 12.3 vol. per cent after its administration, while 5 cases showed a decrease of 11.4 vol. per cent. This indicates that

appeared as though she would recover. This improvement was not sustained and death followed. It is now felt from recent experiments in dogs that this combination glucose and sodium bicarbonate solution may result in a chemical incompatibility of a toxic nature, because death followed its administration in each of the 5 dogs to which it was given. In spite of this unfavorable reaction of the sodium bicarbonate and glucose combination, we still felt the need for a rapid neutralization agent that could be introduced into the circulation without harmful effects.

The literature contains many articles concerning the relationship of acidosis to normal pregnancy and labor. Mention is made of its ever present association in the toxemias. In an attempt to explain this commonly reported finding, a series of blood CO_2 studies in normal labor were carried out, dehydration and starvation acidosis being eliminated by proper fluids and food. The urine of these patients did not show the

TABLE I. CO_2 READINGS ON 157 PATIENTS—FIRST STAGE OF LABOR

PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS
1	51.0	41	40.0	81	40.0	121	44
2	39.0	42	35.30	82	35.0	122	41
3	54.0	43	32.0	83	47.0	123	45
4	43.0	44	46.0	84	30.0	124	38
5	51.30	45	25.0	85	38.6	125	43
6	24.30	46	48.0	86	44.0	126	45
7	45.0	47	49.75	87	43.2	127	44
8	40.0	48	49.0	88	41.75	128	43
9	54.60	49	54.75	89	35.0	129	33
10	46.0	50	37.0	90	39.6	130	33
11	48.0	51	55.30	91	21.6	131	48
12	57.0	52	56.0	92	24.0	132	39
13	48.0	53	42.60	93	41.6	133	44
14	45.0	54	42.60	94	39.0	134	45
15	55.60	55	38.0	95	42.0	135	44
16	50.30	56	51.0	96	43.0	136	52
17	42.0	57	35.0	97	38.6	137	51
18	45.30	58	44.0	98	41.75	138	28
19	38.0	59	43.0	99	43.2	139	44
20	54.0	60	32.0	100	25.0	140	45
21	52.60	61	40.0	101	50.0	141	44
22	38.60	62	48.0	102	43.0	142	52
23	41.75	63	45.0	103	39.3	143	51
24	46.30	64	45.0	104	46.3	144	28
25	39.30	65	44.0	105	50.0	145	48
26	40.0	66	42.0	106	54.75	146	46
27	24.0	67	46.0	107	48.3	147	44
28	26.0	68	53.0	108	40.0	148	51
29	41.30	69	48.0	109	41.3	149	49
30	54.0	70	36.0	110	50.3	150	49
31	42.0	71	44.0	111	46.0	151	37
32	58.6	72	44.0	112	52.0	152	31
33	47.6	73	40.0	113	46.0	153	45
34	44.0	74	43.0	114	47.0	154	43
35	51.0	75	31.0	115	45.0	155	44
36	44.0	76	46.0	116	41.0	156	40
37	35.30	77	42.0	117	48.0	157	44
38	50.60	78	26.0	118	38.0		
39	31.0	79	48.0	119	51.0		
40	37.0	80	31.0	120	46.0		

pulmonary ventilation hyoscine was proved of some value, but mainly because it always intensified the sedation consequently reducing muscular activity. Sodium bicarbonate by mouth was given in a few cases with sodium amytal and hyoscine. The CO_2 was elevated from 4 to 24 vol. per cent, indicating its value as an adjunct with analgesic medication.

Pursuing our original motive, the correction of physiologic acidosis by the administration of soda, it was decided to attempt to combat the

TABLE III. POSTPARTUM CO_2 READINGS

PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS
1	36.0	18	35.3	35	55
2	57.6	19	49.3	36	65
3	51.0	20	29.2	37	48
4	34.0	21	43.0	38	63
5	86.6	22	40.0	39	50
6	36.6	23	35.0	40	65
7	56.3	24	40.0	41	50
8	38.0	25	46.0	42	63
9	52.0	26	35.0	43	42
10	50.0	27	43.0	44	45
11	50.0	28	38.0	45	47
12	48.0	29	44.0	46	51
13	48.0	30	44.0	47	53
14	62.3	31	59.0	48	55
15	46.6	32	47.0	49	42
16	53.6	33	61.0	50	57
17	51.3	34	48.0		

EXPERIMENT 3. EXPERIMENTAL ACIDOSIS PRODUCED BY INTRAVENOUS LACTIC ACID

DOG	CON-TROL	CONDI-TION OF DOG	INTRAVENOUS SOL.	TIME	2ND CO_2	CONDITION OF DOG	DECREASE CO_2
3	56 Vol.	Normal	Lactic Acid	40 Min.	42 Vol.	No effect	14 Vol.
3	42 Vol.	Normal	1%—4 gm.	20 Min.	50 Vol.	No effect	Increase of 8 Vol.
4	56 Vol.	Normal	1%—3 gm.	25 Min.	15 Vol.	Slow respiration	Decrease of 41 Vol.
17	46 Vol.	Normal	2%—14 gm.	30 Min.	29 Vol.	Blood slightly he-molyzed	17 Vol.
17	29 Vol.	Normal	2%—10 gm.	30 Min.	16 Vol.	Slow, deep resp.; irritability	13 Vol.
17	16 Vol.	Normal		40 Min.	16 Vol.	Marked hemolysis. Diarrhea, hemo-globinuria, vom. bl.; recovered	No change
2	50 Vol.	Normal	3%—9 gm.	20 Min.	25 Vol.	Hemolysis-Rec.	25 Vol.
2	25 Vol.	Normal	3%—1.5 gm.	20 Min.	7 Vol.	Died. Hemoglobinuria	18 Vol.

Lactic acid given intravenously produces acidosis. One gram reduces CO_2 4.3 Vol. per cent. A 3 per cent solution in the normal dog produces death. Impending signs: re-spiratory failure and hemoglobinuria with occasional vomiting and diarrhea. The 2 per cent solution aside from a mild hemoglobinuria is without unharful effects. A 1 per cent solution can be used safely and produces the desired acidosis.

TABLE V. SHOWING INADEQUATE ABSORPTION OF SODIUM BICARBONATE BY RECTUM

	NO. HR. OF LABOR BEFORE NaHCO ₃	TIME FROM Na TO 2ND CO ₂	1ST CO ₂	2ND. CO ₂	INC.	DEC.
<i>Administration per Rectum</i>						
1	3'45" PI Mod. Sev.	3 hr. 5 min.	54.0	38.0		16.0
2	7'15" PI Mod. Sev.	10 hr.	35.3	40.0	4.7	
3	23'15" PI Mod.	3 hr.	52.0	45.3		6.7
Aver. 11 hr. Approx.		5 hr. 20 min.	47.1	41.3	4.7	11.3
<i>Administration by Vein to Antepartum Cases—9 Mo. Pregnant</i>						
1	500 c.c. 2%	1 hr. 10 min.	43.0	58.0	15.0	
2	1000 c.c. 2%	2 hr. 40 min.	48.0	65.3	15.3	
Average		1 hr. 55 min.	45.0	60.6	15.1	

EXPERIMENT 5. CORRECTION OF ARTIFICIAL ACIDOSIS BY INTRAVENOUS SODIUM BICARBONATE SOLUTION

DOG	CON- TROL	ACIDOSIS BY LACTIC ACID	TIME	READ- ING	CORRECTED BY SODA SOL. 5%	TIME	READING	CONDITION OF DOG
2	50	9 gm. 3%	20	25 Vol.	25 gm.	15 min.	213 Vol.	Died
		1.5 gm. 3%	20	7 Vol.				
4	56	Lactic Acid	25	15 Vol.	Soda 5%	20 min.	113 Vol.	Good
		14 gm. 2%			15 gm.			
4	113				Soda 5%	25 min.	163	Diarrhea but recovered
					15 gm.			

Dog 2 records the correction of an extreme acidosis of 7 vol. per cent produced by lactic acid and was reversed to an extreme alkalosis of 213 vol. per cent. It is true the dog died, but the result is interpreted in the same manner as previous experiments. Dog 4 a moderated acidosis was corrected by a 5 per cent solution of sodium bicarbonate without any effects. It is certain that a 2 per cent solution would have accomplished the same results without the necessary risk.

EXPERIMENT 6. THE EFFECT OF AN INTRAVENOUS COMBINATION OF GLUCOSE AND SODIUM BICARBONATE. THIS EXPERIMENT WAS DONE TO PROVE THE INCOMPATIBILITY OF THESE TWO DRUGS WHEN COMBINED

DOG	CONTROL	CONDI- TION OF DOG	INTRAVEONUS SOL.	TIME	2ND. CO ₂	END RESULTS
9	50 Vol.	Ether	Glucose 20%	14 HR.	34 Vol.	Died—Bl. Sug- ar 606
13	45 Vol.	Starved	Glucose 20% 100 gm.	50 Min.	84 Vol.	Convulsions
			Soda 2%—Insulin			
13	84 Vol.	Starved	Nothing	45 Min.	52 Vol.	Death
6	42 Vol.	Starved	Glucose 20% 40 gm.	15 Min.	128 Vol.	
		Ether	Soda 5% 10 gm.			
6	128 Vol.		Glucose 20% 20 gm.	15 Min.	148 Vol.	Convulsions
			Soda 5 gm.			
6	148 Vol.		No Sol.	20 Min.	70 Vol.	Death
7	48 Vol.	Starved	Glucose 20% 40 gm.			
		Ether	Soda 10 gm.	20 Min.	112 Vol.	
7	112 Vol.	Same	Same	20 Min.	128 Vol.	Convulsions
7	128 Vol.	Same	Same	45 Min.	85 Vol.	Death

In a series of 8 dogs in which acidosis had been produced by etherization, a combination of glucose solution 20 per cent and sodium bicarbonate 5 per cent were given intravenously. Death followed in each of the 8 dogs. This corroborates our previous clinical impression that this combination is lethally toxic.

WEIGHT CHANGES IN PREGNANCY*

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INTRODUCTION

VARIOUS research workers, especially Cummings,¹ have come to the conclusion that weight changes in pregnancy have a definite relationship to obstetric pathology. Hence this study of weight changes in normal pregnancies was undertaken: (1) To determine whether or not parity, age, and body build are factors in the changes in body weight during pregnancy and the puerperium. (2) To determine whether or not the daily weight changes in the first eight days postpartum are all decreases, whether or not there are any significant differences in them, and if there are significant differences on which days they occur. (3) To determine the total amount of weight change in the first eight days postpartum.

SUMMARY OF THE LITERATURE

In summarizing the literature on the subject, it becomes evident that conflicting results have been obtained from the time of Gassner's² work in 1862. Most workers have thought that parity, body build, and age all affect weight changes in the prenatal and puerperal periods. However, there is considerable variation of opinion on the type and amount of puerperal weight changes. This review of previous work was given in absolute weight changes rather than relative.

The literature on the prenatal period will be analyzed first. The following men, Gassner² (1862), Baumm³ (1887), Lorenzen⁴ (1921), Kemper⁵ (1924), DeLee⁶ (1928), and Trillat⁷ (1928) came to the conclusion that multiparae gained more than primiparae; while Hannahs⁸ (1925) and Cummings¹ (1934) found that primiparae gained more than multiparae. Zangemeister⁹ (1916) found that multiparae and primiparae increased in weight equally from the 29th week on. Siddall and Mack¹⁰ (1933) found that parity had little, if any, influence on the weight changes. The following men, Gassner² (1862), Baumm³ (1887), Zangemeister⁹ (1916), Lorenzen⁴ (1921), Kemper⁵ (1924), Mahnert¹¹ (1924), and Kerwin¹² (1926) found that heavy women gained more than light. None of the work showed the reverse, that the light women gained more than the heavy. Siddall and Mack¹⁰ (1933) came to the conclusion that body build had little, if any, influence in weight changes. The following workers, Lorenzen⁴ (1921), Kemper⁵ (1924), and Siddall and Mack¹⁰ (1933) found that the young women gained more than the old. None of the workers were of the opposite opinion, that the old women gained more than the young.

Next the literature on the puerperal period will be analyzed. The following men, Gassner² (1862), Baumm³ (1887), and DeLee⁶ (1928) came to the conclusion

*This study was submitted to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Obstetrics and Gynecology.

livery, and febrile puerperium. As a starting point in the weight history the patients stated their normal nonpregnant weight, wearing their usual house clothes. Usually the patients had been weighed within a short time before they became pregnant.* During the prenatal period the patients were weighed with clothes on every two weeks until the last month, and every week during the final month. These prenatal weighings were done on the usual pound and ounce lever scale, and the results converted into kilograms.

The weighings just before delivery and during the puerperium were taken on a very delicate Henry Troemner scale. This scale was graded in the metric system, and was constructed like the instruments used in quantitative chemistry. The scale guarantee was that of a sensitivity of plus or minus 5 gm. with a load under 300 pounds. Actually, however, it was found to be more sensitive than this, as changes down to a gram were registered.

One woman was weighed at a time. A wheel litter was used in transporting the patient to the scale. The top of the litter was detachable from the four-wheel frame. Four chains were hung from one end of the scale bar, and these snapped onto the litter top. This top, a blanket, and a perineal pad were first carefully balanced to zero by means of a bucket of fine lead shot hung from the other end of the scale lever bar. The patient was then placed on the litter top, wearing the perineal pad, and covered only by the blanket. The litter frame was pushed away, so that the actual weighing was only of the patient, as everything else had been previously balanced to zero. The method of weighing was the same as that used in quantitative chemistry, taking a certain number of oscillations, averaging and finding the dead center.

Sixty-nine women were weighed on this accurate scale just before delivery, immediately after delivery, and at the same time each afternoon during their hospital stay. They were given a thorough enema before delivery, and their bowels were kept open after delivery. Five of the women, however, insisted on going home on the seventh postpartum day, so that only 64 cases were completed. All component products of labor were weighed on a smaller metric lever scale. The products consisted of fetus, placenta, fetal urine and stool, mother's urine and stool, and blood (a small additional remainder of the blood had to be estimated). The remaining difference between predelivery and immediate postdelivery weight covered amniotic fluid and moisture lost by skin evaporation and respiration of mother.

*I gained the impression that the patients were not guessing as to their weight, but had been weighed within a month or so before becoming pregnant. This meant that the weights were probably accurate within the limits of ordinary commercial scales which are found in grocery stores and drug stores.

that multiparae lost more than primiparae. The reverse, that primiparae lost more than multiparae, was found in one phase of Kemper's⁵ work (1924). Heil¹³ (1896) found that para i, iii, iv, and v lost less than the average, while para ii lost more than the average. The following, Gassner² (1862), Baumm³ (1887), Heil¹³ (1896), and DeLee⁶ (1928) came to the conclusion that heavy women lost more than light. The reverse, that light women lost more than heavy, was found in one phase of Kemper's⁵ work (1924). In comparing the weight changes between old and young in the puerperium, Heil¹³ (1896) found that in the youngest and oldest groups, the weight loss was under the average. Kemper⁵ (1924) found a great diversity of results according to what groups were compared. First, he analyzed the first twelve puerperal days. He found in comparing the heavy elderly multiparae and the light young primiparae, that the heavy lost more than the light, the elderly more than the young, and the multiparae more than the primiparae. In comparing the heavy young multiparae and the light old primiparae he found, also, that the heavy lost more than the light, the old more than the young, and the multiparae more than the primiparae. However, he found that heavy old multiparae lost more than light old multiparae, the light old primiparae lost more than heavy old primiparae, the heavy young multiparae lost more than light young multiparae, and heavy young primiparae lost more than the light young primiparae. When Kemper⁵ compared the weight losses of delivery plus the first twelve puerperal days, he found the heavy lost more than the light, the old more than the young, and the primiparae more than the multiparae.

Gassner² (1862), Baumm³ (1887), and Heil¹³ (1896) were the only authors who stated whether or not the immediate puerperal weight changes were all decreases. Gassner² (1862) and Baumm³ (1887) found the puerperal weight changes to be all decreases. Gassner² (1862) carried his figures through the eighth day postpartum and Baumm³ through the sixth day postpartum. Heil¹³ (1896) found from the eighth postpartum day on there was an increase until the thirteenth day, when he discharged his patients. (He frequently had a very small secondary reduction on the ninth, tenth, or eleventh day.)

Significant differences in the daily puerperal weight changes were shown in the work of Gassner² (1862), Baumm³ (1887), and Heil¹³ (1896). Heil¹³ (1896) found a definite augmentation of loss on the first, fifth, and sixth days. Gassner² (1862) found a definite augmentation of loss on the first day, then a more or less gradual diminishing loss. Baumm³ (1887) found a definite augmentation of loss on the first and fourth days, with a gradual increasing loss on the fifth and sixth days.

The total amount of weight change in the immediate puerperium of the various authors, will next be analyzed. Gassner² (1862) found a loss of 4.868 kilograms in eight days. Heil¹³ (1896) found a loss of 1.700 kilograms in eight days. Zangemeister⁹ (1916) found a loss of 1.61 kilograms in seven to twelve days. Kemper⁵ (1924) found a loss of 1.261 kilograms in twelve days.

From this review and summary it becomes apparent that there is: (1) only a small amount of previous work, (2) a great conglomeration of conflicting ideas and opinions as to the effect of pregnancy and the puerperal state on the weight of women, (3) a complete lack of sufficiently accurate work to measure small changes in weight correctly, and (4) a complete lack of statistical evaluation of the weight changes.

METHOD OF COLLECTING AND ANALYZING DATA

Since the purpose of this study was to measure the physiologic changes in body weight of women during the prenatal and puerperal periods, care was taken to exclude all cases of toxemia, abnormal de-

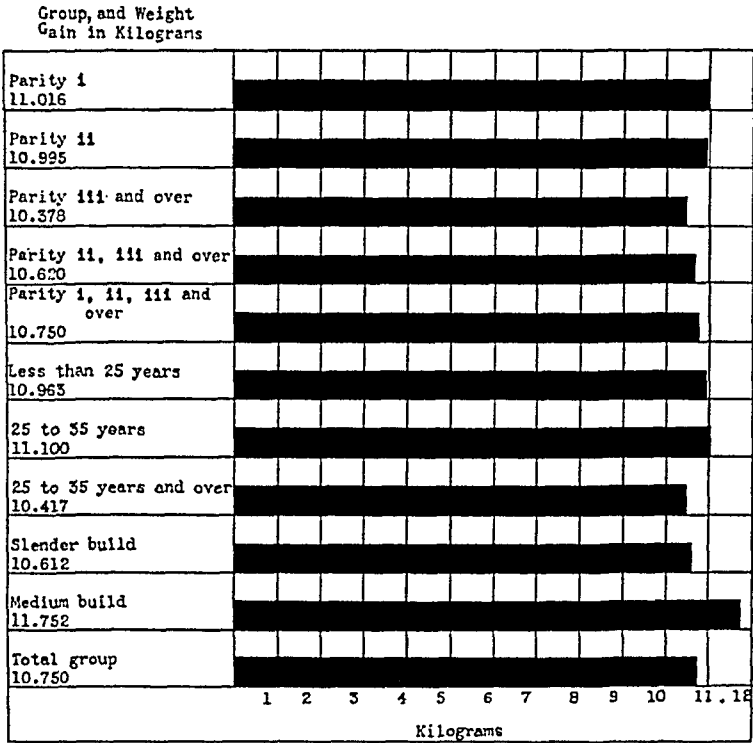


Chart 1.—Graph made of the means of the total weight gains in kilograms during the prenatal period.

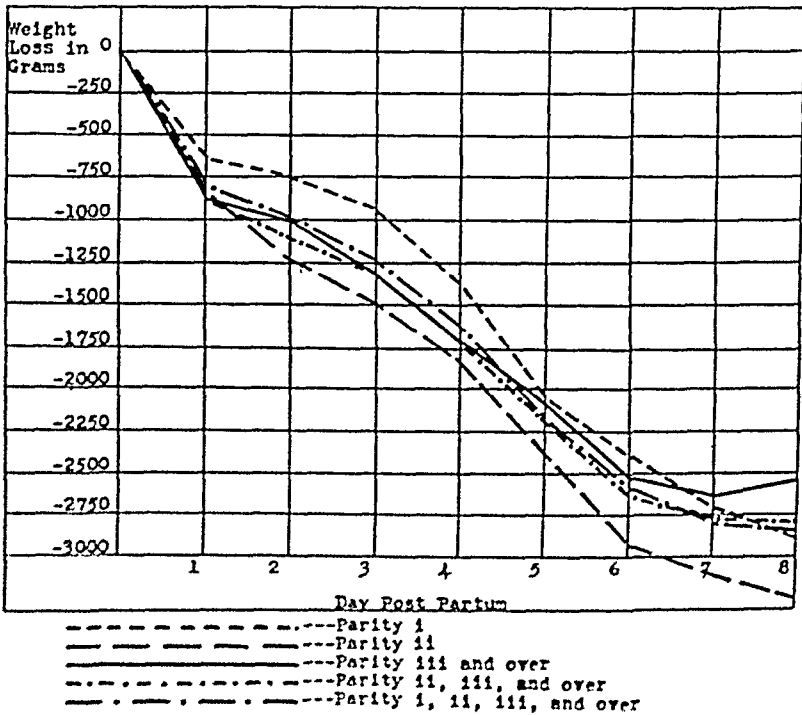


Chart 2.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to parity. 0, the first (immediate) postpartum weight.

For purposes of comparison and study, the basic data were divided into a number of groups.

The first division was according to parity, first into three groups: para i, para ii, para iii and over, and second into primiparae (para i) and multiparae (para ii and over).

The second division was according to three age groups, young less than twenty-five years, medium twenty-five years to thirty-five years, and old over thirty-five years.

The third division was according to three groups of body build: slender, medium, and stout. The slender group included all women under two pounds per inch of height, medium from two pounds to $2\frac{1}{2}$ pounds per inch of height, and stout all cases of $2\frac{1}{2}$ pounds and over per inch of height. Since there were only 5 cases in the stout group subsequent comparisons were limited to those between the slender and the medium groups. Also, since there were only one slender and one medium weight woman over thirty-five years, these two cases were omitted. Consequently, the weight comparisons in this group were made up of women in the slender and medium weight groups, under thirty-five years of age.

The mean weights and their standard errors were computed by the usual statistical methods for each one of these subgroups. The difference between any two means was tested for significance by the ratio of the difference to its standard error, that being the commonly used relative deviate.

When R is 2.0, such a difference between two means would occur for two samples from the same population only 5 in 100 times. When R is 3.0, such a difference would occur between two samples from the same population only 1 in 100 times. According to common statistical practice a difference is considered significant when it would not occur by chance oftener than 1 in 100 times, i.e., when R is 3 or more. Some workers consider a R of 2.0 as indicating a possibly significant difference. Since P , the probability integral, indicates the chances in unity, P times 100 equals the chances in 100. The means for the various groups are given in Charts 1 to 5.

RESULTS

According to the figures in Chart 1, parity makes no difference in the increase in body weight of pregnant women, since in this series none of the differences between the means had relative deviates as large as 2.0. Similar analyses showed the same lack of difference in prenatal increase in weight for age and body build. The chart shows that the mean increase in weight during pregnancy is 10,750 kilograms. Too much reliance cannot be placed on this figure because of the unknown sources of error in the measurement of preconception weight of the women.

Likewise, age does not affect the daily postpartum changes in weight (Chart 3), as none of the differences between the means for the same day in the age groups had relative deviates as large as 2.

With body build only one difference between the mean daily weight changes for slender and medium build (Chart 4) had a relative deviate between 2 and 3, all others being less than 2. Therefore, body build also had no influence on postpartum decrease in weight.

The mean daily weight changes of the whole group for the first eight puerperal days were next compared to each other as shown in Chart 5. These changes show that they are all decreases. The decrease for the first day is significantly greater than that for any other day with the

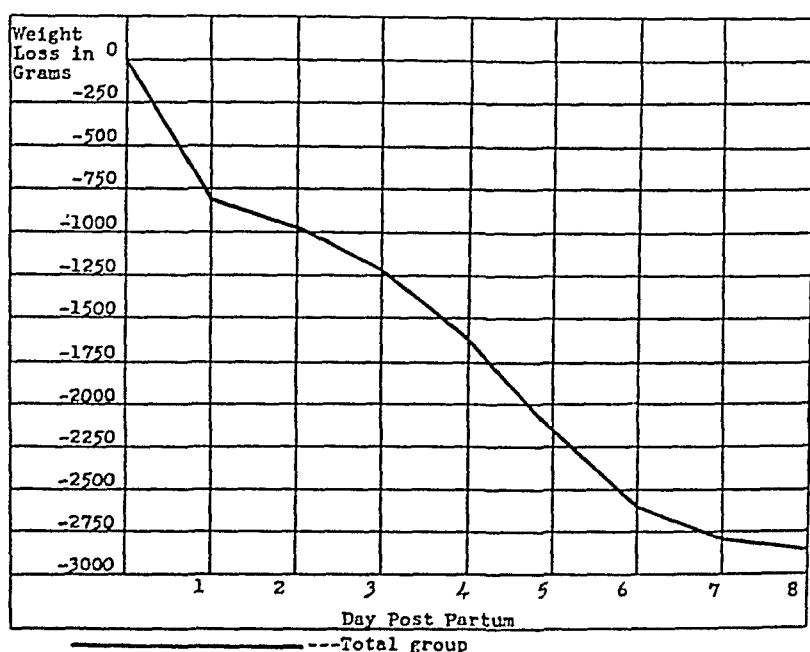


Chart 5.—Summary graph made of the means of all the cases.

possible exception of the fifth day, when the relative deviate of 2.7 indicates a possibly significant difference. Also, the decrease for the fifth day tends to be significantly greater than that for all days except the two adjacent ones, the fourth and sixth. These differences indicate that the postpartum decrease in weight is not regular, but instead is largest (0.8 kilo.) on the first day, drops to 0.2 kilogram on the second day, then increases to 0.5 kilo. by the fifth day, and decreases again to the low level of 0.06 kilo. on the eighth day. The significance of the differences between the decrease for the first and other days, and between the fifth and most other days, indicated that there is a true augmentation of the postpartum decrease on the first and fifth days.

The total amount of decrease in weight for the whole group in the first eight puerperal days was 2.831 kilo. \pm 0.140 kilo.

According to the values given in Chart 2, parity makes no difference in the changes in mean daily weight during the puerperal period, since none of the differences between means for the same day had relative deviates of 3 or more. (There were three differences that had a relative deviate between 2 and 3, but all the rest were less than two.)

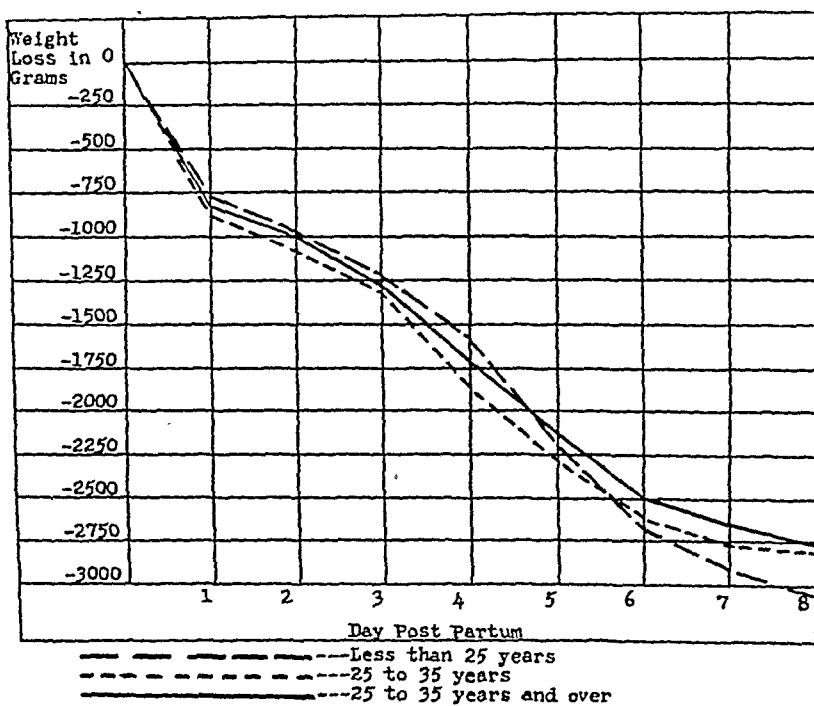


Chart 3.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to age. O, the first (immediate) postpartum weight.

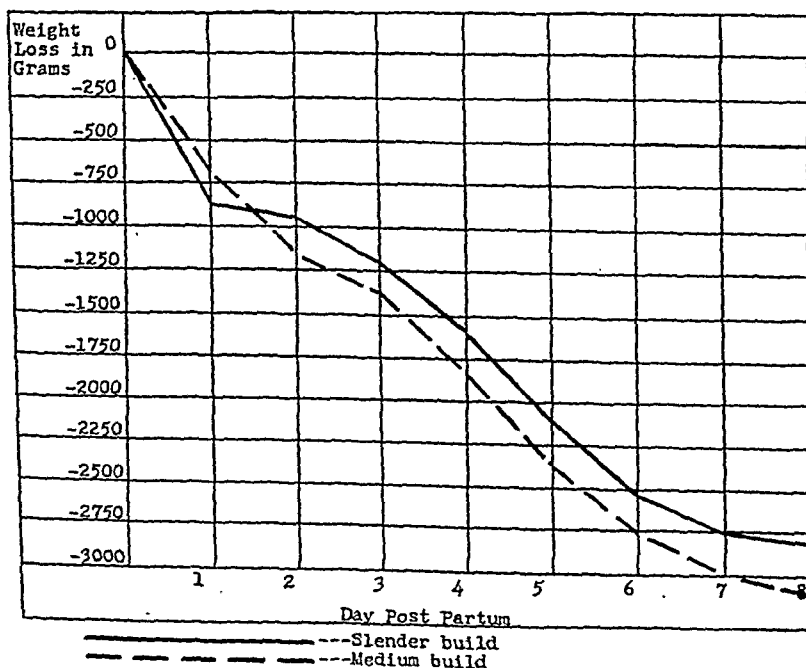


Chart 4.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to body build. O, the first (immediate) postpartum weight.

WHEAT GERM OIL THERAPY

III. RAT EXPERIMENTS, LACTATION, CLINICAL USES, "FAILURES," AND EFFECT UPON CONGENITAL ANOMALIES

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RAT EXPERIMENTS

AS WAS mentioned in a previous publication,¹ female rats fed on an E-free diet developed in two to four months the classical evidences of E-deficiency, viz., the habit of resorbing their fetuses. At the same time their blood serum revealed the presence of the antiproteolytic estrogenic factor for the first time. On the other hand, in normal control rats this was not the case. That report indicated that 88 per cent of a group of 16 rats showing sufficient deficiency of vitamin E to cause all their fetuses to be resorbed revealed the presence in their sera of this antiproteolytic power, whereas only 5 per cent of a group of 20 rats given vitamin E or fed on approximately normal diets, or on E-defective diets for too short a time to become E-free, or normally fed male rats, revealed such power. Since that paper appeared, we have tested more rats under the same circumstances and now can report that our total figures should be respectively 93 per cent of a group of 30 rats and 11 per cent of a group of 28 rats. The accuracy of the test is well illustrated by these figures.

LACTATION

Another feature of interest is the fact that 16 of our 60 patients, who during pregnancy displayed an excess of the estrogenic antiproteolytic substance in the blood, and required wheat germ oil in order to reach term, had an unusual amount of milk secretion just after delivery. One primiparous patient had 8 ounces of milk available for each nursing for days, and another primipara easily produced 7 ounces or more for each nursing. Another primiparous woman had so much secretion on the day after delivery that she soaked her clothing and bed, as a few women do on the fifth to tenth days postpartum. Surprisingly enough, we have noticed no tendency for this exaggerated milk secretion to continue beyond the first seven to ten days postpartum. Indeed, after that time five of these 16 women experienced genuine difficulty in providing adequate quantities of breast milk for their infants. On the other hand, 5 of our patients treated with the oil throughout pregnancy had a

DISCUSSION

This statistical analysis of new data has failed to substantiate earlier opinions that parity, age, or body build has an effect upon the increase of weight during pregnancy and the decrease of weight in the puerperium. Only Siddall and Mack¹⁰ have found similar negative results as to the effect of parity and body build, and Zangemeister⁹ as to the effect of parity on weight variations in the prenatal period. However, Siddall and Mack¹⁰ did think that age was a factor, the younger women gaining more than the older.

There has been a tendency, similar to the findings in this analysis, to note the major decrease in weight in the puerperium on the first and fifth or one of the two adjacent days. As previously stated, Heil¹³ found an augmentation of loss on the first, fifth, and sixth days, Gassner² on the first day, and Baumm³ on the first and fourth days with a gradual increasing loss on the fifth and sixth days.

The total decrease in weight in the first eight days of 2.831 kilo. \pm 0.140 kilo. in this study falls intermediate between the low value of 1.700 kilo. found by Heil¹³ and the high value of 4.868 kilo. found by Gassner.² Obviously, the amount of decrease would be materially affected by differences in diet and management of puerperium.

SUMMARY AND CONCLUSIONS

1. Parity, age, and body build are not factors in the changes in body weight of women during the prenatal period and the first eight days of the puerperium.

2. The daily weight changes during the first eight puerperal days are all decreases, there being significant augmentations of loss on the first and fifth days.

3. The total mean weight loss in the first eight puerperal days is 2.831 kilo. \pm 0.140 kilo.

I am indebted to Dr. Jennings C. Litzenberg and Dr. John A. Urner of the Department of Obstetrics and Gynecology for advice concerning the problem, and to Dr. Edith Boyd of the Department of Anatomy for assistance in statistical analysis.

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CLINICAL USES

Should every pregnant woman take wheat germ oil? One suspects the answer should be in the affirmative. It has long been recognized that a very high percentage of pregnancies in both America and Europe terminate prematurely, whether by act of nature or human intervention. It would appear that the greater proportion of these abortions are natural, for the success of widely known abortifacient medicines taken orally and known by the whole profession to be inert, suggests that abortion was impending when these drugs were taken and that their success was largely a triumph of coincidence. If we were to admit that even one-tenth of conceptions were in danger of premature spontaneous interruption, the widespread use of wheat germ oil early in gestation might seem to be justified. If, however, there be added to this indication for its use the beneficial effects achieved by it in the prophylaxis and therapy of abruptio placentae,⁴ and if that complication of pregnancy occurs as commonly as Goodall would have us believe,⁵ and as I also feel,⁶ then there is some reason to advise the use of vitamin E therapy in every pregnancy. In the past four years I have had no habitual aborters in my private practice, but have treated 12 miscarriages and 17 abortions with wheat germ oil. Miscarriage was prevented in 91 per cent and abortion in 88 per cent of the group of patients so treated. The therapeutic success with the whole group of 29 cases therefore averaged 89 per cent.

The effect of the oil in stimulating defective lactation in a certain percentage of women has been indicated earlier in this paper.

If it is true that vitamin E acts largely through its antagonism to estrogenic substances in the blood, then it should have a place in the therapeutic fields now occupied by pregnancy urine gonadotropic hormone, thyroid extract and progesterone. In a previous paper⁷ we suggested that it might be of use in treating defective male patients, as had been suggested earlier by Moench.⁸ We produced testicular descent in a boy by means of its use after a long trial with a pregnancy urine gonadotropic substance had failed to help. We have used it successfully in a very small number of cases of dysmenorrhea which were associated with a high blood content of estrogenic substance, based on the analogy between its action and that of progesterone. Vaginal and anal pruritus⁹ have been helped by it in women whose blood showed estrin excess.

One does not feel that its usefulness as a therapeutic agent has been exhausted by any such list as the above. Undoubtedly many more pathologic entities will be found to be associated with an excess of estrogenic material in the blood, and will be materially helped by therapy directed toward the correction of such excess.

minimal amount of lactation from the very beginning, drying up before the third day. To sum up, 36, or 60 per cent, of the 60 patients treated with wheat germ oil during their pregnancies were able to nurse their babies for three months or longer, and 5 had very defective lactation from the first. Sixteen, or 27 per cent, at the beginning exhibited an unusual amount of secretion. As a control series we may refer to the nursing records of our last 60 patients who carried pregnancies to term without the use of wheat germ oil. Thirty-five, or 58 per cent, of the 60 were able to nurse their babies, and 18 had very poor lactation from the very beginning. Only 7 exhibited evidences of an unusually large amount of milk secretion.

It is known, of course, that estrin is responsible for nipple development and the proliferation of the duct system of the breasts. The mammatropic hormone from the anterior lobe of the pituitary gland, which is directly responsible for milk secretion, comes into full play when the estrin of the body has been excreted in the puerperium, and this is supposed to be fairly complete by ten days, or even sooner.

Sure² showed that rats kept on a diet deficient in reproductive vitamins, but bred so soon after being put on this diet that they could deliver live young, could rear these up to the fifteenth or seventeenth day of life. Then lactation suddenly became inadequate and the young reached a weight plateau and soon perished. The administration of wheat germ oil to the mother rats, however, soon enabled lactation to proceed adequately and many young were saved. He believes the lactating mothers had depleted their reserves of the lactation-promoting fraction of vitamin E and required the ingestion of more before further nursing could be accomplished. Later³ he indicated that both the antineuritic and growth-promoting fractions of vitamin B are important for adequate lactation in rats. With this work of Sure's in mind, we have tried large doses of wheat germ oil in the effort to stimulate lactation in 23 women in the puerperium. All were patients who could not produce more than 4 ounces of milk per day in spite of every effort that could be made. Fifteen of the 23 had taken wheat germ oil during their pregnancies. Of these 10 patients we were successful in inducing adequate lactation in 6 and failed completely in 4. Of the other 8 we had success with 2. Altogether the successes were 8 in 23 cases, or roughly 35 per cent.

The patients who were successfully treated thus for inadequate lactation reported definite tingling of the breasts appearing in about five or six hours after the administration of an ounce of the oil. The breasts were well filled with milk before twenty-four hours had elapsed, but treatment had to be kept up for about two weeks on the average. If it were stopped, lactation ceased, only to start up just as before when the oil was taken again. Sure remarked that rats required about twice as much oil for lactation as for reproduction, but this did not appear to be true in this small group of women we have studied.

The number of our cases is too small to warrant any inferences, except that it seems as if a brief trial with a large dose of wheat germ oil might be indicated in those women who evince defective lactation in the puerperium.

abortion or who had taken absurd draughts for the same purpose and been pleased by their success. Indeed Tate¹⁵ has recently reported obtaining in the blood of a criminally aborting woman the same findings as in those of women who abort spontaneously, and which strongly suggest an excess of estrogenic substance. Mall¹⁶ years ago observed that only one of 82 cases of abortion, from which specimens were sent to him and which were found to be so deformed that abortion was very likely, did not give a history of intervention to induce the abortion. Mall and Meyer observed that abortions ascribed to influenzal and other infections "remind one of the defective fruit which persists insecurely upon the tree until a sudden gust of wind showers it to the ground." We suspect that such factors are in great part of secondary importance, and would be ineffective if the patient were saturated and controlled properly with vitamin E.

To indicate the trend in recent opinion one may point to the work of Moussu¹⁷ who has had considerable success in prophylactically treating endemic abortion in cattle, formerly ascribed almost exclusively to infection with *Bacillus abortus*, by means of wheat germ oil.

The author has had six instances of failure among his own patients including three premature deliveries of live children. One of these failures is included in the Watson and Tew report. In this case the blood serum was normally digestible at the time of the premature delivery. One patient aborted at the second month whose blood serum did not show any evidence of deficiency of vitamin E and on whom wheat germ oil therapy had no effect that could be discerned. The decidual cast strongly suggested that there had been an attempt at the formation of a placenta previa. In the other four cases the blood serum showed evidence of E-deficiency at delivery, however. In one of these four the patient had neglected to take her wheat germ oil for three days before she suddenly went into labor. One patient had been deliberately taken off the oil in June of 1936 and put on a green diet in the hope it might prove to be an adequate substitute. Before the mistake could be rectified her membranes had ruptured and she had gone into premature labor. In the other two cases the wheat germ oil used was very old and had become slightly rancid. In these last four cases the antiproteolytic factor had re-appeared in the blood serum at the time they went into premature labor. This is at least a very striking coincidence.

The literature would suggest that lettuce, spinach, water cress, and other such green foods rich in vitamin E can be used as a substitute for the latter when plentiful. That can be true only to a very limited extent. The author each spring and early summer for three years has attempted just such a substitution and been compelled to admit failure. Some of his patients, as has been mentioned, went into labor prematurely, and others threatened to do so. All of them showed a return of the antiproteolytic estrogenic factor in the blood in the course of a week or so

FAILURES WITH WHEAT GERM OIL THERAPY

From what has gone before, it can be seen that many of the failures with wheat germ oil therapy have their origin in factors which are readily controllable. That there is a considerable percentage of failures cannot be denied.

Vogt-Möller¹⁰ in his series of 23 cases reported that 78 per cent of the patients went to term and 87 per cent delivered viable children. Watson and Tew¹¹ in 53 cases reported 72 per cent success. More recently Currie¹² has reported 86 per cent of his 35 cases carried successfully to term or beyond the fifth month at the time his report was sent to press. Nicholson in discussing his paper mentioned that two patients whom she had treated had not had a successful outcome. The author in a series of 44 cases of spontaneous abortion¹³ (as well ascertained as such cases can ever be) and 26 cases of spontaneous miscarriage¹⁴ found in the whole group 74 per cent which showed E-deficiency or excess of the antiproteolytic estrogenic factor in the blood serum. As stated earlier in this paper, the author has treated 29 patients with threatened abortion or miscarriage with wheat germ oil with 89 per cent successful outcome at term. There still remains a considerable percentage of cases, ranging from 28 to 11 per cent, in which vitamin E therapy has appeared to be inadequate, but one suspects this should not constitute more than 15 per cent.

As has been indicated, failure with this mode of therapy may be ascribed to inadequate dosage, personal idiosyncrasies leading to inadequate assimilation, associated hypothyroidism, failure to allow for seasonal depletion of the body depots of vitamin E, rancid oil which has been kept at too high a temperature or allowed to deteriorate with age. Of course, we must add the very important and obvious fact that many abortions may not be due to E-deficiency or excess of estrogenic antiproteolytic substance in the blood at all, but to other factors such as infection, trauma, sperm abnormality, etc.

Once our patients are under control with wheat germ oil we allow them to take long automobile rides or do heavy work without regard to the previous precarious character of the pregnancy. We have never had any untoward results from this practice. Indeed one of our women with a threatened abortion, which was controlled by a massive dose of wheat germ oil, slipped on the stairs and descended a flight of four steps, sitting heavily on each step in doing so. There was not the slightest trace of a relapse in her condition and she had a normal delivery at term. Another case of partial abruptio placentae at the fifth month of pregnancy had her pain promptly controlled by two massive doses of wheat germ oil. On the next day she was cystoscoped for a complicating pyelitis, and did not abort.

We suspect that the reverse is also true, viz., that many of the causes of abortion and miscarriage commonly accepted as such are of only secondary importance and could never provoke a threatened or actual interruption of pregnancy unless there was a background of deficiency of vitamin E. We have repeatedly found such a deficiency in the blood sera of women who had used ridiculously ineffectual measures to induce

fects such as spina bifida or hairlip, while the fetus is still plastic and one can hope that correction is at least theoretically possible. We do not propose to enter into any detailed discussion of these two points in this paper. Our views will be published later in more detail.

However, one can often detect spontaneous abortion before it develops by means of the author's test for a disturbance of the relation between vitamin E and estrogenic substance in the blood serum. In the hope that some success would attend a study of this equilibrium in those pregnancies which later delivered deformed infants, we tested a large number of blood samples taken in the first trimester of pregnancy, especially from women who had had anomalous fetuses previously. Our series is small, but is presented for what suggestive value it may have.

Five women who later delivered deformed infants were tested in the first trimester of pregnancy. All showed estrogenic excess and deficiency of vitamin E in their blood sera. Six out of 8 (or 75 per cent) of defective pregnancies first tested in the second trimester showed the same result. In short, where such a disturbance in the relation of vitamin E to estrogenic substance is found, one may suspect, at least, that the fetus is deformed. That deficiency of vitamin E is a factor in producing fetal deformity is strongly suggested by the studies of Macomber²³ and Byerly and his coworkers.²⁴ That vitamin B₁ is also a factor appears from the report of Slonaker,²⁵ and that estrogenic substance is involved is indicated by Kozelka and Gallagher.²⁶

What will wheat germ oil, rich in both E and B₁, accomplish if given very early in pregnancy in cases in which there is marked probability that the fetus is abnormal? He would be bold who would presume to answer that question with assurance. A colleague, Dr. A. E. Mowry, had a patient whose only conceptions had resulted in two successive anencephalic infants. Before the third conception and throughout the whole of that pregnancy she was given enough wheat germ oil to control the estrogenic substance in the blood. She delivered a normal child at term. Murphy²⁷ has pointed out that where there is one defective child, the next child has twenty-four times as much chance of being deformed as a child chosen at random in the general population. With the background of two identical deformities in the siblings, the chance of this third conception having a normal outcome must have been very small indeed.⁸

There is an unusually marked tendency for harelip to be repeated in siblings, it is believed. The author had a patient whose first conception ended in a very severe cleft-palate and harelip at term. As soon as she conceived again, her blood was found to be defective in vitamin E and

*Through the courtesy of Dr. A. Sinclair of Sebringville, Ontario, I can present the report of a patient who had had in her first two pregnancies a seven-month hydrocephalic fetus and a full-term spina bifida, respectively. She was first seen by him at the sixth week of her third pregnancy and promptly put on wheat germ oil therapy. She delivered a normal child at term.

The author reported in a previous paper¹ the appearance of two hydrocephalics in the litters of his E-defective rats. Recently Barrie has confirmed and extended this observation independently. (*Nature* 139: 286, 1937.)

after the oil therapy had ceased. Probably so much of this estrogenic substance is in circulation in these precarious cases that a great deal of a concentrated form of vitamin E, viz., wheat germ oil, is required to prevent it from harming the pregnancy.

EFFECT UPON CONGENITAL ANOMALIES

It has long been recognized that many spontaneous abortions and miscarriages are associated with developmental anomalies of the fetus. This was best illustrated in the extensive studies of Mall and Meyer¹⁶ at the Carnegie Institute.

Beckwith Whitehouse¹⁸ mentioned two instances of deformed infants born at term after abortion had been averted. Moench⁸ states that it is often not worth while to try to save the products of gestation nature is trying to get rid of, on account of the chance that the child will show developmental defects at birth. Mall and Meyer quoted a remark of Bacon who said he had delayed an abortion in two or three instances in which a monster had been delivered at term. Nageotte-Wilbouchewitch¹⁹ reported two examples of threatened abortions which were carried to term only to produce idiots, and two threatened miscarriages which when carried to term or near term produced respectively an infant with a malformed chest and one with a congenital scoliosis. Kane,²⁰ among thirty-six living children whose mothers were habitual aborters, found that five were congenitally defective, and thought that the prevention of abortion in the early months of pregnancy merely prevented nature's elimination of the unfit. He suggested that fetal anomalies might be due to hormonal deficiency.

Some people may feel, therefore, that the prevention of abortion and miscarriage by means of adequate wheat germ oil therapy is a misdirected effort.

Falls,²¹ however, using progesterone therapy was able to carry 83 per cent of his group of 41 cases of threatened or habitual abortion to viability. All that were carried to term were normal, but two of his failures were cases in which abnormal fetuses were expelled. Currie¹² carried 21 cases of habitual abortion to term with wheat germ oil therapy and notes that one of these died of a "structural deformity of the throat." Whitehouse¹⁸ mentions a woman delivered prematurely of a spina bifida in her second pregnancy, who was carried to term in her third pregnancy by means of wheat germ oil. The normal baby delivered in this third pregnancy was born with a dimple over the lower spine. Neither Vogt-Möller,¹⁰ Juhász-Schaffer²² nor Watson and Tew¹¹ have reported fetal anomalies in the infants brought to term by them under the influence of wheat germ oil. Of the 29 cases of threatened abortion or miscarriage carried to term on wheat germ oil by the author, one infant developed soon after birth a mild type of spasticity of the legs, which has persisted. This patient had no oil until the fifth month. Another woman, who was first seen at the fourth month with so much amniotic fluid that the fundus uteri was at the level usual for six months, was put upon wheat germ oil at the fifth month, carried thus for two months, then x-rayed. As a deformed child was detected, labor was induced and a fetus with craniorrhachischisis was delivered.

It is obvious, of course, that the prime desiderata in this problem are a means of detecting fetal anomalies before at least the twelfth week of pregnancy and a means of correcting certain types of developmental de-

EPILEPSY AND PREGNANCY

A REVIEW OF THE LITERATURE AND A STUDY OF THIRTY-SEVEN CASES

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THE relationship between epilepsy and pregnancy is of interest to the obstetrician from three separate angles. First, does the disease influence the course of the pregnancy in any way, and vice versa; second, what are the probabilities of the transmission of this affliction to the offspring; and third, what are the means for differential diagnosis between an epileptic seizure and an eclamptic convulsion? References to this problem are rather difficult to find in medical literature and available references for the most part consist of statements of opinion without statistical study.

The admission of a pregnant epileptic patient to the Baltimore City Hospital Obstetrical service aroused considerable interest in this problem from the viewpoint of the obstetrician. The paucity of information in the literature and the inconsistency and inadequacy of the published opinions are somewhat discouraging, and thus it seems appropriate to study the problem thoroughly with hope of throwing some light on this question, particularly of how the obstetrician may best serve the interests of his epileptic patient. This was attempted by first reviewing the literature to date and then by studying all the available case histories of epileptics in the files of the three largest obstetric clinics in Baltimore.

The first observer to mention the relationship between epilepsy and pregnancy was Echeverria, a student of epilepsy, who in 1867 published a treatise on this disease in which he stated that his general impression was that gestation usually has a favorable influence on the frequency of the epileptic fits but he gives no statistics. It is interesting and important that in those days the criteria for the presence of epilepsy in the family background were very inaccurate, and the following list represents the conditions which when found in the family history were considered positive evidence of an hereditary background: hysteria, neurasthenia, insanity, migraine, obsessions, tic, stuttering, temper, periodic headache, tuberculosis, chorea, bilious attacks, morphinism. E. M. Bridge has recently pointed out that such a miscellaneous assortment of diseases obviously is an extremely inaccurate criterion to use in a series of statistics to establish the transmission of epilepsy. In 1885 Reynolds, another student of epilepsy, reported a statistical study on 1,450 cases from the National Hospital of Paralyzed and Epileptic and found that in this series there were 785 female cases and in 7 of these cases the first fit occurred during pregnancy and in 5 others the first convulsion was observed a very short while after delivery.

The first pertinent reference to the effect of pregnancy on epilepsy appears in the German literature in 1889 when Nerlinger in a dissertation at Strassburg stated that 50 per cent of epileptics are improved by pregnancy but no statistics are offered to support this contention. In 1901 Gowers published a series of statistics which comprised 3,000 cases of epilepsy, 52 per cent of which were females and he reported that in 10 of these cases the initial attack of epilepsy occurred during a pregnancy. First in the *American Textbook of Obstetrics*, published in 1899, stated,

high in estrogenic substance. She was promptly put on wheat germ oil, and had an uneventful pregnancy and normal child at term.

A patient of ours, who showed all the classical signs of partial abruptio placentae in the sixth month of her first pregnancy, was carried to term on wheat germ oil. She delivered a baby that appeared to be typically Mongolian. Yet the baby appears to have normal or better than normal intelligence. It is now twelve months old.

Enough has been said, perhaps, to indicate an approach to the problem of congenital anomaly in the human being that offers some hope. At least it indicates a fertile field for further study.

SUMMARY

1. Ninety-three per cent of 30 rats kept on a diet defective in vitamin E until they began to resorb their fetuses possessed antiproteolytic power in their blood serum. Only 11 per cent of 28 rats on normal diets revealed this substance.

2. In 35 per cent of 23 women whose lactation was inadequate during the puerperium, wheat germ oil therapy restored efficient lactation.

3. Some of the therapeutic possibilities of wheat germ oil are indicated.

4. About 15 per cent of abortions are not controlled by wheat germ oil therapy. Failures are discussed.

5. As so many aborted fetuses are deformed, the question arises as to the advisability of wheat germ oil therapy designed to prevent abortion. Statistics are reviewed, and personal experiences recorded, to indicate that such therapy is probably justified.

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because sometimes this aggravates the attacks. Furthermore, if the mother were to have an attack while the baby were nursing at the breast the child might be seriously hurt. In some cases pregnancy aggravates epilepsy and in these instances further conception should be prevented by contraception or by a sterilization operation." Here again it is interesting to note a general statement of opinion and a hurried statement concerning the exceptions. And again, another textbook rather dogmatically stating the deleterious consequences of the effect of nursing on the course of the disease. One suspects that these dogmas may be perhaps begged, borrowed, or stolen from one text to another.

The question of the hereditary factor in epilepsy has undergone some drastic changes of outlook in recent years with such men as William Lenox of Boston and others compiling critical statistics on the incidence of epileptic heredity. Although there still remains much work to be done in this field the recent studies point to the conclusion that the incidence is not nearly so great as it was assumed to be not very long ago. In the most recent edition of the *Oxford System of Medicine*, Lenox very convincingly reports an exhaustive and thorough statistical study which reveals an heredity incidence of about 10 per cent, and he concludes that this may be a generous figure.

In this connection one other point comes to mind. How much is the mild epileptic patient with normal mentality influenced by the superstition, mystery and stigmas associated with this affliction in the minds of most laymen? Who knows but that this influence itself may contribute somewhat to the mental changes which are observed in many epileptics as they go through life, looked upon by many of their fellow men as being "possessed of a demon." Dostoevsky, the famous Russian literary genius, himself an epileptic, paints a vivid picture in his book *The Idiot* of an epileptic during a seizure and also points out the unfavorable and unhealthful light in which the epileptic himself realizes he is being viewed by society. Unfortunately, until very recently students of this disease drew their conclusions from studies of institutionalized patients, which group is by far the minority of epileptics. Bridge, in 1930, with this point in mind showed that studies including noninstitutionalized private patients reveal a less foreboding outlook.

From the reports obtained from the literature to date it is obvious that the relationship between epilepsy and pregnancy has not engaged the attention of physicians to any great extent. It seems appropriate, therefore, at this time to study a series of case histories in the hope of shedding some light on the problem and this was attempted by making a survey of the case records from the three largest maternity clinics in Baltimore, namely, The Baltimore City Hospital, The University of Maryland Hospital and The Johns Hopkins Hospital.

Epilepsy has not been indexed in the records of these three hospitals during certain years and some case records, particularly the early ones, leave much to be desired. Nevertheless, records were found of 37 patients treated in the obstetrical clinics of these institutions which were diagnosed as pregnancy complicated by idiopathic epilepsy. The cases have been studied particularly from the standpoint of the effect of pregnancy on the epilepsy and with the exception of 3, the cases seemed to

"Epilepsy is a rare complication of pregnancy and as a rule does not influence unfavorably the course of gestation. Convulsions are often absent during pregnancy and sometimes do not make their appearance until after the child is weaned." It is interesting to bear this opinion in mind and contrast it with a statement of opinion made in Williams' *Textbook of Obstetrics* in 1903. On the subject of epilepsy Williams concluded, "The disease appears to have no effect upon pregnancy though at the time of labor it may be mistaken for eclampsia by inexperienced observers. If the attacks are frequent the patient should be put upon large doses of potassium bromide and treated just as at other times. As a rule it is not advisable to allow the mother to nurse her child, as lactation sometimes appears to aggravate the disease while serious injury might possibly be done to the child during an attack. On the other hand, in occasional instances the mentality of the patient appears to undergo progressive deterioration with each succeeding pregnancy. In such circumstances pregnancy should not be interrupted but the advisability of sterilization after delivery should be considered."

Sachs of Germany in 1910 published his opinion to the effect that pregnancy has no predictable influence one way or another on epilepsy. He dogmatically stated, however, that status epilepticus when it occurs during pregnancy is always fatal to both mother and child. About ten years ago there was considerable material to be found in the German literature on the relationship between epilepsy and eclampsia. Poten in 1925 wrote on this subject and concluded that both were really one and the same disease while Zangemeister partially shared this view and in 1926 went on record as believing that 2 per cent of eclamptics are left suffering from epilepsy as a residual.

Waldstein's interest in this question was keenly stimulated by a case of his own at the Womans Hospital in Vienna. He published this case report in 1928 together with a review of the French and German literature to date on the case reports of 23 epileptics. These 24 women had 54 pregnancies, 40 of which ended spontaneously at term, 4 prematurely, and 10 as early abortions. Waldstein concluded from this study that 50 per cent of epileptics are improved during pregnancy. He held to the belief that epilepsy and eclampsia are separate and distinct diseases.

In Australia, in 1927, at a meeting of the Victorian Branch of the British Medical Association, A. E. Fraser presented a case which stimulated some interesting discussion relevant to the problem of pregnancy in the epileptic patient. The consensus regarding the question of the transmissibility of epilepsy was that heredity was not so pronounced a factor as was generally supposed.

In 1928 in the *Journal of the American Medical Association*, Williams published an article entitled "Indications for Therapeutic Sterilization in Obstetrics." This was a summary of the indications for sterilizations that had been done in his clinic up to the time of publication of the article. There were three patients sterilized because of epilepsy, and when discussing this indication he stated, "Each year a number of epileptic women pass through our hands and we have gained the impression that, in general, epilepsy has no effect on pregnancy or vice versa. Nevertheless, we have sterilized 3 patients sent to us by the psychiatrists with the statements that one had suicidal tendencies and that all showed signs of mental deterioration and that it was probable that the continuation of pregnancies would hasten the process." At the present time so far as I can gather from conferences with the psychiatrists of the same clinic that referred the above mentioned patients to Williams they are not by any means convinced that pregnancy has any predictable influence on epilepsy.

In 1931 Struthers of London reported three cases of epilepsy which had their onset associated with pregnancy and none of these patients had a family history of epilepsy or any suggestive personal past history, and in 1934 Hayden reported his case of a known epileptic who had a convulsion during the second stage of labor. The child was born alive and in good condition. In the *Practitioners Library of Medicine and Surgery*, published in 1936, Greenhill states, "Epilepsy usually has no effect on pregnancy or labor but it may be mistaken for eclamptic convulsions. Treatment is the same as in the nonpregnant state. Nursing should be forbidden

during a subsequent gestation if any occurred. The average frequency of attacks before gestation was once monthly and during the pregnancies the average frequency was once every six months. This improvement cannot be accounted for by the institution of sedative therapy because in only one of these cases was this done early in gestation, and in that case the frequency of the attacks after delivery was approximately the same as before conception. One fact, however, seems significant in the histories of this group; in 4 of these there was a definite relation between the epileptic seizure and menstruation. The association of epilepsy with menstruation is a matter of common medical knowledge, and because of the intimacy of menstruation and reproduction, an attempt was made to determine from each history in this survey whether or not the patient's attacks were associated with the menses. In 7 of the cases there was a definite relationship and 4 of these fell into the improved group and 3 in the group which revealed no change. One suspects that a larger series may reveal a definite tendency toward improvement during pregnancy in this type of case, which might well have a logical physiologic rationale. This group is well illustrated by the following case:

G. B., colored, with a generally contracted rachitic pelvis and a negative epileptic family history, began to have typical epileptic fits at 13 years of age, once each month close to the menstrual period. At the age of 19 she became pregnant and during gestation she had only 3 seizures, one each in the second, fifth, and sixth months. She was delivered at term of a normal living child by elective cesarean section because of cephalopelvic disproportion. On the sixth post-partum day she had 3 epileptic convulsions (the child was not breast fed). Following this episode she was put on daily luminal therapy and she had one convulsion two months post partum when her menses appeared. Four months after delivery she again became pregnant and had no attacks throughout the gestation. She was again delivered of a normal child at term by cesarean section and sterilized by tubal ligation, and the puerperium was free from attacks. Although she was instructed to return for a follow-up, she was never heard from again.

Four patients fell into the group which were made worse by pregnancy. Two were primiparas and 2 were multiparas whose average frequency of attacks in the nonpregnant state was every six weeks and during pregnancy was every two weeks. In none of these cases was there any relation between the attacks and menstruation. The following case is representative of this group:

M. T., white, whose mother gave a history of grand mal attacks which occurred at irregular intervals since the puerperium of her first pregnancy. There was no change in the frequency of the mother's attacks throughout 3 subsequent pregnancies. The patient gave a history of petit mal attacks "all her life," described as fleeting attacks of fainting preceded by feelings of unreality, occurring irregularly. At the age of 24 she had two typical grand mal attacks within one week, and subsequently the petit mal attacks occurred as before until the age of 26 when she became pregnant. During the first six months of gestation she had 8 grand mal attacks spaced at fairly regular intervals. She was put on daily luminal, and during the last four months of pregnancy had 3 major seizures. At term she was delivered spontaneously of a living normal child and the puerperium was uncomplicated except for a major epileptic fit on the third, fifth, and twelfth days (child not breast fed). During the following eighteen months she had 4 major seizures but no petit mal attacks, and then became pregnant again. During this second gestation a

fall into one of 4 separate groups; those in which there was no effect; those made worse; those which were improved and a fourth group in which the onset of the epilepsy was associated with pregnancy. The more interesting facts are set down in Table I, and a few individual cases are recorded as representative of each group.

TABLE I. CLASSIFICATION

	NUMBER OF CASES	NUMBER OF PRIMIPARAS	NUMBER OF MULTIPARAS	AVERAGE AGE YEARS	AVERAGE AGE ONSET OF EPILEPSY YEARS	EPILEPSY RELATED TO MENSES	AVERAGE FREQUENCY OF ATTACKS	AVERAGE FREQUENCY OF ATTACKS
							NON-PREGNANT	PREGNANT
No change	21	10	11	25	14	3	Every two weeks	Every two weeks
Improved	5	5	0	20.6	14.2	4	Monthly	Every six months
Worse	4	2	2	23.2	12.3	0	Every six weeks	Every two weeks
Began with pregnancy	4	2	2	19.5	19.5	-	0	Every two months
Unclassifiable	3	1	2	25.6	?	?	-	-

The most conspicuous fact revealed in the study is that a considerable majority (21), of the cases fell into the group in which the pregnancy had no effect on the epilepsy. There were 10 primiparas and 11 multiparas in this group and the average frequency of the attacks was every two weeks. Conversely, in no case in the entire series did the epilepsy have any effect on the pregnancy except in those cases in which the disease was misinterpreted as eclampsia and delivery was unnecessarily radical. This mistake was made in 5 of the 37 cases in the series and the patients treated as eclamptics. The following case illustrates that group in which the epilepsy was not influenced by the pregnancies and also brings out the possibility of a wrong diagnosis:

A. R., white, with a negative epileptic family history, began to have convulsions at the age of 15 years. The attacks appeared irregularly but averaged one seizure every two to three weeks. At the age of 20 she became pregnant and throughout gestation there was no change in the frequency of the attacks. One week before term a convulsion occurred, and she was hospitalized. Although the blood pressure was normal and the urine contained only a trace of albumin, a diagnosis of eclampsia was made and labor was induced with a Vorhees' bag. After a four-hour labor she spontaneously delivered a full-term, living normal child. The history of previous fits was not obtained until after labor was induced. She was put on luminal therapy and did not suckle the child and the puerperium was uncomplicated except for a typical epileptic seizure on the fifth day. On continuous luminal and bromide therapy, the attacks continued every two or three weeks. At the age of 22 years she became pregnant again and was delivered spontaneously at term of a living child in the same clinic. The frequency of the attacks still remained unchanged when she was seen at a one-year follow-up, not pregnant. Both children were apparently normal at that time.

Five of the patients in the study were definitely improved during their first pregnancy. Unfortunately none of these patients were seen again

the differential diagnosis of eclampsia and epilepsy alone, excluding the possibility of convulsions of other etiology, one in every four pregnant women having convulsions should be an epileptic. We should refrain, therefore, from jumping to conclusions too readily when we see a pregnant patient in a convulsive seizure. Treatment by sedation is, of course, of value in either condition but the prognosis is alarmingly different.

CONCLUSIONS

From the reports and opinions available and the facts revealed in this study, it appears that the following attitude may justifiably be taken by the obstetrician:

Epilepsy has no appreciable effect on the course or termination of a pregnancy.

The reports of the effect of pregnancy on epilepsy are both conflicting and confusing. The investigation of 37 case histories indicates that there is no general rule by which we can be guided, although in the majority, pregnancy has no effect on the epilepsy. Therefore, like so many other problems in obstetrics, the treatment and disposition of the pregnant epileptic will depend upon the merits of each individual case, and it seems that the number of patients who will require special handling will be in the minority.

In the light of recent clearer knowledge the obstetrician may be of infinite help to his pregnant epileptic patient; first, by dispelling the mysterious superstition which surrounds the disease he may establish a more helpful, less pessimistic attitude of mind regarding her own outlook. Next, he should assure her that the probability of the transmission of the disease to her offspring is not so great as she probably thinks it is.

One final conclusion seems more certain. By specifically inquiring about the occurrence of seizures suggesting petit mal or grand mal at the first prenatal visit we may spare ourselves a subsequent "pseudo-eclamptic" surprise.

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major epileptic attack occurred about every three weeks on luminal therapy. She delivered a full-term child spontaneously and the puerperium was free from attacks. She was followed no further.

The fourth classifiable group comprises those patients whose initial attack of epilepsy was associated with pregnancy. There were 2 primiparas and 2 multiparas; in none of this group was there a family history of epilepsy and nothing suggesting petit mal in their personal past history. In 3 of the cases the seizures began during the first pregnancy and occurred at irregular intervals thereafter. In the other case the fits occurred in the puerperium of the second pregnancy and is here recorded to illustrate this group:

R. V., colored, with negative past history was delivered spontaneously at term at the age of 16. Again at term she was delivered spontaneously at the age of 17 and two days postpartum had a typical epileptic convulsion (the child was breast fed). The attacks occurred irregularly during the next seven years and in this interval she had 5 normal term children and there was no change in the epilepsy throughout these gestations. During her eighth pregnancy the attacks disappeared entirely and remained absent for the following six months, when at the age of 26 she became pregnant for the ninth time. During the first twelve weeks of this pregnancy she had 26 convulsions at approximately regular intervals. During this episode sedative therapy gave no relief and therapeutic abortion and sterilization were done. At a six-week follow-up she reported 3 convulsions since the abortion. She was not heard from again.

Three cases in this study were placed in an unclassifiable group because these patients were idiots with arrested mentality, and it was impossible to gain any information from the histories. However these patients delivered infants that were apparently normal.

Aside from the information given in the table the following facts were revealed by this study: The years in which epilepsy was indexed in the hospitals surveyed represent a total of 54,688 patients treated, an incidence of 0.067 per cent. The fetal and maternal mortality was zero, and so far as they were followed, the babies were apparently normal.

The clinical characteristics of the convulsion, per se, will not serve to differentiate eclampsia from epilepsy. It must also be remembered that the blood pressure may be temporarily elevated during an epileptic seizure and the convulsion is frequently followed by a moderate albuminuria. The postconvulsive coma of eclampsia usually appears deeper and more prolonged than that following an epileptic attack and the hypertension more persistent. The presence of edema with marked hypertension and urinary changes point toward eclampsia but the most valuable differential point, however, is the history of epilepsy, writ large. In some cases even this will not hold as the present study reveals that the number of cases in which the initial epileptic attack is associated with pregnancy is slightly higher than would seem to be coincidental. In a recent survey of eclampsia over a five-year period in the entire state of Maryland, Reese and Peyton found an incidence of 0.2 per cent or one case of eclampsia in every 500 deliveries, while in the survey included in this paper the incidence of epilepsy complicating pregnancy is 0.067 per cent or one case in every 1,500 deliveries. Eclampsia, then, occurs three times as often as epilepsy in pregnant women, so that, in

estrin.^{4, 8} After recording these motility responses, the rabbits were sacrificed and each uterine horn dissected free and weighed. The amount of enlargement taking place in each instance was determined by comparing the weight of the distended horn (empty) with the corresponding undistended horn from the same rabbit. Sections from each uterus were also taken for histologic study. Under the foregoing conditions the following results have been obtained:

Spontaneous Motility.—Three of the distended uteri were highly active, showing a succession of major contractions of varying durations and frequencies. Although the uteri were highly active, the motility was characterized by great irregularity (arrhythmicity), as shown by the examples in Fig. 2. This motility stands in marked contrast to the regular or rhythmic type of uterine motility which follows the administration of estrin (Fig. 3). The undistended or control uterine fistulae showed no measurable motility (cf. Rabbit 4, Fig. 2), although the

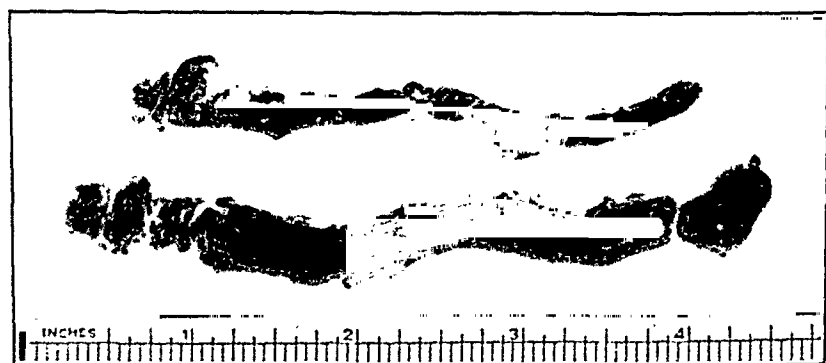


Fig. 1.—Uterine cornua from Rabbit 4. Dissected free and fixed in formol-acetic fixative. Top, undistended cornu; bottom, emptied cornu after four days of chronic distention with fluid. Weights, 3.27 gm. and 9.11 gm., respectively. See Fig. 2 for motility records.

balloons in the two uteri were of the same size and under the same distending pressure (20 cm. of water).

The experimental horns in the remaining three rabbits were almost completely inactive; they showed very feeble, irregular activity which was little different from that seen in the control horns. The latter were quiescent, as is normally the case this length of time after ovariectomy.³ Consequently, no uterine motility was induced in these three rabbits by the distention method employed in these experiments. The amount of uterine enlargement which took place is described below. Suffice it to say now that motility was induced in only three of the six rabbits although appreciable uterine enlargement occurred in the distended uteri of all the rabbits. Clearly, therefore, the motility observed in these experiments depends upon some factor other than uterine growth resulting from the stimulus of distention; this factor was found to be local inflammatory processes, as noted below.

UTERINE MOTILITY RESULTING FROM INFLAMMATORY PROCESSES IN THE MYOMETRIUM, IN THE ABSENCE OF OVARIAN HORMONES*

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AT THE present time it is generally held that one may induce motility of uterine muscle in ovariectomized rabbits in only one way,^{3, 5} namely, by the injection of ovarian follicular hormone or other estrogenic agents. When it was found, however, that suitable degrees of chronic distention of the uterus elicit hypertrophy⁶ and hyperplasia¹ of the myometrium of ovariectomized rabbits it seemed likely that one would find motility associated with these structural changes. Although distention did not induce motility, it was found that, in certain experiments in which inflammatory processes were present, uterine motility was induced. The procedures were as follows:

Six mature, isolated rabbits were injected with prolan in order to bring all the animals into a comparable state of pseudopregnancy. On the seventh day, the ovaries were removed and one week later, uterine fistulae were prepared in the usual manner.³ At this time, a ligature was passed about the tubal end of the left uterus in each case. On the third day following this operation, the left uterine cornu was distended with physiologic saline (2 or 4 c.c.) without aseptic precautions. In order that the saline would be retained, a purse-string suture was passed about the orifice of the uterus which was exposed in the preparation of the fistula. The fluid was allowed to remain in place until the fourth day later; at this time the growth-effects of chronic distention are about complete.⁷

As a result of these procedures, six rabbits were available at the end of the third week after ovariectomy, each one of which possessed one uterine cornu (left) developed in response to chronic distention and another uterine cornu (right) which was undistended and undergoing atrophy of castration (Fig. 1). Such atrophying uteri are invariably nonmotile and are unreactive to the usual oxytocic agents, except epinephrine.⁸

The spontaneous motility of both uterine cornua in each rabbit was simultaneously recorded from the unanesthetized rabbits on the fourth day after distention and the reactivity to pilocarpine and epinephrine determined. Pilocarpine was used, since in the experience of one of us it is effective only on uteri that are motile under the influence of

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in contrast to the responsiveness to this drug of the estrin-activated uterus. Typical epinephrine responses were regularly obtained, however, indicating the recording capability of the technical procedures in each case.

Motility in Relation to Growth and Histologic Changes.—The percentage increases in size of the distended uteri over the nondistended uteri ranged from 18 per cent at one extreme to about 189 per cent at the other. Marked motility was observed in uterine cornua showing 18 per cent, 178.6 per cent, and 189.2 per cent increases in size. The relatively nonmotile or feebly active experimental uteri showed percentage increases of 75.6 per cent, 106.4 per cent, and 108.3 per cent, respectively. Consideration of these results will show that the motility which was induced by distention is not dependent upon growth changes taking place, since the uterus showing least growth was highly active and, conversely, appreciable enlargement occurred in the three nonmotile uteri. Examination of the histologic changes which are associated with the occurrence of motility in these experiments has proved fruitful, however.

The control or undistended uteri in all cases presented a picture of castration atrophy such as has been described.⁶ The cells were small, the cytoplasm densely staining; the glands were inactive and the tissues relatively avascular. The experimental uteri presented a contrasting picture: the cells were large, the nuclei vesicular, the cytoplasm increased in amount, the tissues more or less edematous, and the epithelium of the endometrium was tall columnar in type and actively secreting. The growth responses were particularly prominent in the myometrium of all the experimental uteri. Inasmuch as three of these were quiescent, however, it is clear that growth resulting from chronic distention is not, per se, a stimulus for myometrial activity. The nonmotile uteri were free of inflammation, except in the most superficial portion of the endometrium. In striking contrast to this observation is the fact that inflammatory changes were a conspicuous feature in each of the active uteri, being especially prominent in the vascular zone of the myometrium. Here, marked hyperemia was observed and prominently associated with this in each case was the infiltration of large numbers of polymorphonuclear cells throughout the tissues. Although these cells were most numerous in the superficial portions of the endometrium they were also present in considerable numbers in the tissues about the vascular zone in the myometrium. In the inactive experimental uteri this inflammatory condition of the myometrium was conspicuously absent.

DISCUSSION AND SUMMARY

When the uterine fistula of an untreated, ovariectomized rabbit was distended with fluid for four days, growth of all the tissue components took place. *In the absence* of irritative changes in the myometrium, no

Reactivity to Pilocarpine.—Five to 6 mg. of pilocarpine-HCl were injected intravenously once or twice in each rabbit. The usual elevation of tone which one sees in estrin-treated rabbits receiving pilocarpine was lacking in every instance in the present experiments, even in those uteri showing considerable activity. A characteristic uterine response to pilocarpine in an estrin-treated rabbit is shown in Fig. 3, and the absence of such an effect in the present experiments is shown in the

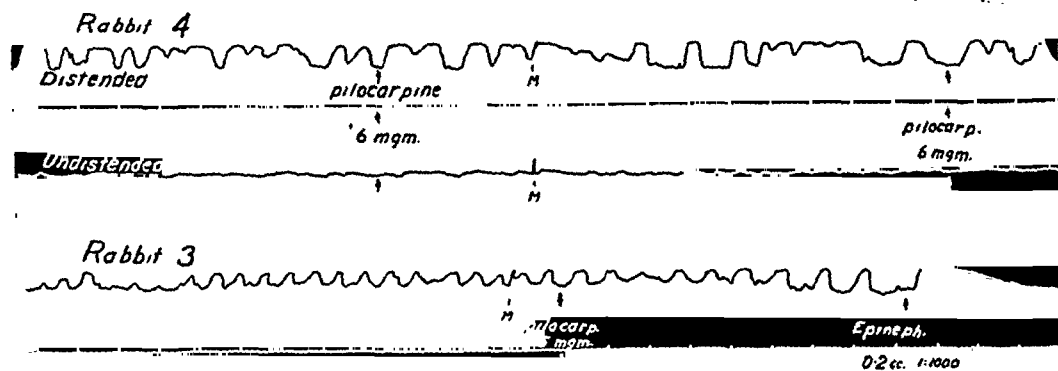


Fig. 2.—Uterine motility in untreated, ovariectomized rabbits (unanesthetized) whose uteri were distended for four days with fluid. Motility was observed when there were inflammatory conditions in the myometrium but not otherwise, even though growth resulted from the distention. Note lack of regularity of contractions and lack of uterine response to pilocarpine. Time, minutes.

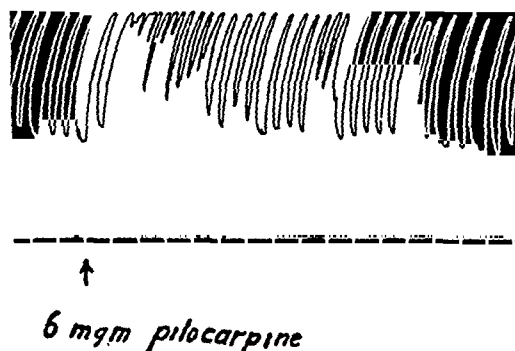


Fig. 3.—Uterine motility in estrin-treated rabbit, unanesthetized. Note the regularity of the contractions and the response to pilocarpine lasting for more than four minutes.

records of Fig. 2. The pilocarpine was effective otherwise in these rabbits, however, since excessive salivary and lachrymal gland stimulation occurred and a large amount of fecal material was passed after each injection.

In summary, it may be said that the motility which was induced by inflammation in these uteri differed in two respects from that which follows the injection of estrin in ovariectomized rabbits. First, it lacked coordination and rhythmicity characteristic of the estrin response, and second, the distention-activated uteri were unresponsive to pilocarpine

ANALGESIA DURING THE FIRST STAGE OF LABOR

FURTHER STUDY OF DILAUDID-SCOPOLAMINE

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OF THE 755 cases in this series, I¹ reported 101 cases, taken in part from private practice and in part from the obstetric service of the University of Tennessee Medical School, in May, 1934. The remaining 654 cases are all from private practice.

Our previous study was essentially a comparison of dilaudid-scopolamine and morphine-scopolamine as to speed of action, quality of analgesia in the mother and depressive symptoms in the baby. Our results were so definitely in favor of dilaudid-scopolamine that we continued to use it in all of our cases. In view of our further experience with this combination, an analysis of all our results with it seems desirable at this time. In the present series, dilaudid in combination with scopolamine was used exclusively for first stage seminarco-sis and various types of anesthesia (ethylene, nitrous oxide, ether) were used for the second stage. In part of the series, nembutal and sodium amytal were used in 3 and 6 gr. doses, respectively. In some cases where the patients were extremely nervous and apprehensive, these barbiturates were given early, preceding the use of the dilaudid combination, and in others it was given later, where the patient had become restless, for a greater degree of narcosis.

The results of the combined series have been outlined in tabular form to show the time elapsing between the original dose of the drugs and the breathing of the baby, the quality of narcosis obtained in the mother, and the effect of the drug upon the baby. No attempt has been made to indicate the para nor to outline the number of doses given of either drug, nor the exact dosage in each individual case.

By the term "slight asphyxia" as used in the tables we mean simply a slight delay of twenty to forty seconds in the cry or breathing of the baby. Perhaps the word "apnea" as used by Eastman² is a better term for this condition. All of these babies began to breathe after removing mucus from the throat or following minor resuscitative measures, such as gentle rubbing of the back or thumping of the feet. The term "deep asphyxia" as used in the tables was applied to babies who showed prolonged asphyxia and included the stillborn babies as well as those who had asphyxia livida or asphyxia pallida.

uterine motility was observed. Accordingly, neither chronic distention and the associated anabolic changes which resulted therefrom, nor the balloon, the presence of which constituted a "foreign body" within the uterus when the motility was being studied, were motility-provoking agents. In the cases in which motility was observed, histologic evidence of inflammation in the myometrium was present. This consisted of marked hyperemia of the vascular zone, edema of the tissues, and infiltration of the uterine tissues with polymorphonuclear cells.

It was found that the features of the motility obtained under the conditions of these experiments differed in two ways from that which results from the administration of estrin to ovariectomized rabbits. In the first place, the motility which is associated with inflammation of the myometrium in these experiments is arrhythmic, whereas that which follows the injection of estrin is rhythmic. In the second place, uteri which were motile because of an associated inflammatory condition of the myometrium were found to be unreactive to pilocarpine administration in amounts which were highly effective in estrin-activated uteri. The nature of these differences between the two types of motility remains to be elucidated.

It may be pointed out in conclusion, however, that both types of motility have one feature in common. The uterine motility which results from the action of estrin is preceded by marked hyperemia and edema of the uterine tissues,^{2, 5} and in the present experiments motility is observed when marked hyperemia and edema of the vascular zone in the myometrium occur. Investigation of the rôle of hyperemia in the initiation of uterine motility should prove fruitful.

We are indebted to Howard R. Gerber for technical assistance in these experiments.

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In 1923 Mondor and Huet reported only 38 known cases of mucous cysts of the labia minora. The author adds an observation of his own. The author feels with Schauta and Kollmann that although wolffian body rests have not been demonstrated in this area, it is possible that there might be an alteration of wolffian epithelium in this area to form a mucous cyst.

MARIO A. CASTALLO.

TABLE III. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE NO_2O_2

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT AS-PHYXIA	DEEP AS-PHYXIA
Less than one hour	12	3	9	12	0	
One to two hours	16	16	0	15	1	
Two to three hours	34	34	0	33	1	
Three to four hours	36	36	0	36	0	
Four to five hours	50	49	1	48	2	
Five to six hours	19	19	0	19	0	
Six to seven hours	13	13	0	12	1	
Seven to eight hours	10	10	0	10	0	
Eight to nine hours	14	14	0	13	1	
Nine hours and over	15	14	1	13	0	2 Still-born
Total	219	208	11	211	6	2

In this group of 58 cases, nembutal (3 gr.) and sodium amytal (6 gr.) were given late in labor for restlessness and 7 babies (12 per cent) showed slight asphyxia, and there were none with deep asphyxia.

TABLE IV. FIRST STAGE BARBITURATE AND DILAUDID-SCOPOLAMINE. SECOND STAGE NO_2O_2

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT AS-PHYXIA	DEEP AS-PHYXIA
Less than one hour	2	2	0	2	0	
One to two hours	2	2	0	1	1	
Two to three hours	4	4	0	2	2	
Three to four hours	8	8	0	7	1	
Four to five hours	4	4	0	4	0	
Five to six hours	4	4	0	3	1	
Six to seven hours	6	6	0	6	0	
Seven to eight hours	4	4	0	4	0	
Eight to nine hours	2	2	0	2	0	
Nine hours and over	22	22	0	20	2	
Total	58	58	0	51	7	

The patients of this group received ether anesthesia in the second and third stages following dilaudid-scopolamine first stage analgesia. There were only 18 in this group, and out of this number 11 (61 per cent) showed slight asphyxia livida and 3 breathed normally only after several minutes of resuscitation and the administration of carbon dioxide-oxygen. It is interesting to compare the ether group with those receiving other anesthetics for the second and third stages. In the 737 patients receiving ethylene or nitrous oxide, a delay in cry or breathing, in no case lasting over forty seconds, occurred in 31 cases (4.2 per cent). Only where ether was used was there any marked asphyxia and there is no doubt in our minds that it was the offending factor.

Since smaller doses of dilaudid as well as of scopolamine had been reported,³⁻⁵ for obstetric or surgical analgesia, we varied the size of the dose of both drugs in a number of cases. A combination of $\frac{1}{32}$

In the 270 cases of this group, all had dilaudid-scopolamine during the first stage and ethylene-oxygen for the second and third stages. Good analgesia was obtained in 235 of the cases; the remaining 35 obtained only fair analgesia. In 254 of the babies (94.1 per cent) crying and respiration were spontaneous. Slight asphyxia was present in 15 babies (5.6 per cent). There was one stillborn baby who had asphyxia pallida due to an intracranial hemorrhage resulting from a rapid second stage in a multipara.

TABLE I. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE ETHYLENE-OXYGEN

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT AS-PHYXIA	DEEP AS-PHYXIA
Less than one hour	0					
One to two hours	45	15	30	45	0	0
Two to three hours	0					
Three to four hours	45	45	0	35	10	
Four to five hours	60	60	0	59	0	1 Still-born
Five to six hours	70	67	3	66	4	
Six to seven hours	50	48	2	49	1	
Seven to eight hours	0					
Eight to nine hours	0					
Nine hours and over	0					
Total	270	235	35	254	15	1

In this series of 75 cases nembutal (1½ gr.) and sodium amytal (3 gr.) were given interchangeably prior to the administration of dilaudid-scopolamine. The resulting analgesia was good in all cases and only 3 babies (4 per cent) exhibited slight asphyxia and none had deep asphyxia.

TABLE II. FIRST STAGE BARBITURATE AND DILAUDID-SCOPOLAMINE. SECOND STAGE ETHYLENE-OXYGEN

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT AS-PHYXIA	DEEP AS-PHYXIA
Less than one hour	0					
One to two hours	0					
Two to three hours	0					
Three to four hours	30	30	0	29	1	
Four to five hours	20	20	0	20	0	
Five to six hours	22	22	0	21	1	
Six to seven hours	3	3	0	2	1	
Seven to eight hours	0					
Eight to nine hours	0					
Nine hours and over	0					
Total	75	75	0	72	3	

All of the 219 cases summarized in Table III had dilaudid-scopolamine in the first stage and nitrous oxide-oxygen in the second and third stages. The general analgesic effect in this group was good and only 6 babies (2.7 per cent) showed slight asphyxia. Two babies were stillborn as a result of a prolonged period of "molding" in primiparae followed by asphyxia pallida.

symptoms. In all but 4 or 5 babies the lungs were completely expanded at the end of three to five days. The only baby who showed definite symptoms of atelectasis clinically failed to clear up within the few days' period, but was all right at the end of one month. Several babies who showed slight atelectasis in the x-ray pictures were from mothers who had no seminarcosis during the first stage.

SUMMARY

In a series of 755 cases, $\frac{1}{32}$ gr. of dilaudid and $\frac{1}{130}$ gr. of scopolamine proved to be a satisfactory combination for the production of seminarcosis during the first stage of labor, providing a pleasing analgesia for the mother with little, if any, effect on the baby. In some cases a small dose of one of the barbiturates was administered in conjunction with dilaudid-scopolamine analgesia. When ethylene or nitrous oxide was used for anesthesia in the second and third stages, apnea occurred in only 4.2 per cent of the babies. With ether, respiratory difficulty was encountered more frequently.

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EXPERIMENTAL TRANSPLANTATION OF THE OVARIES

AUTOTRANSPLANTS OF DOG OVARY INTO OMENTUM

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SINCE the publication of the preliminary report by the author,¹ in which a brief summary of the literature was listed, there has continued widespread and increasing interest in the subject of ovarian transplantation. The recent literature adds little that is really new, but serves to crystallize the knowledge of the subject. An excellent review of the subject can be found in the Report of the French Surgical Association (XLV Surgical Congress), published in 1936.²

In this communication we report further experimental studies done with autotransplants of dog ovary into the omentum. In the preliminary report we presented the histologic findings of autotransplants and homotransplants which had been removed for study after three months.

It is generally known that functional transplanted tissue of a few weeks' duration may at a later date present an entirely different picture with disappearance of most, if not all, of the functional elements; that

TABLE V. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE ETHER

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT AS-PHYXIA	DEEP AS-PHYXIA
Less than one hour	0					
One to two hours	0					
Two to three hours	6	6	0		4	2
Three to four hours	2	2	0		2	
Four to five hours	0					
Five to six hours	0					
Six to seven hours	2	2	0		1	1
Seven to eight hours	2	2	0		2	
Eight to nine hours	0					
Nine hours and over	6	6	0	4	2	
Total	18	18	0	4	11	3

gr. of dilaudid and $\frac{1}{130}$ or $\frac{1}{200}$ gr. of scopolamine was used (Burrhoughs-Wellcome hyoscine hydrobromide was used throughout the series). Likewise dilaudid $\frac{1}{48}$ gr. was used with $\frac{1}{130}$ or $\frac{1}{200}$ gr. of scopolamine. We were unable to see any advantage in the smaller doses of either dilaudid or scopolamine, and since no ill effects were noted in this study, we are satisfied that for a patient of average weight the dosage used in the technique outlined in our previous report is the proper one. This method is as follows: $\frac{1}{32}$ gr. of dilaudid and $\frac{1}{130}$ gr. of scopolamine are administered subcutaneously when the cervix is dilated $3\frac{1}{2}$ to 4 cm. in primiparae and $2\frac{1}{2}$ cm. in multiparae; forty-five minutes later, $\frac{1}{130}$ gr. of scopolamine; forty-five minutes later, a dose of $\frac{1}{260}$ gr. of scopolamine, repeated again in forty-five minutes, and thereafter every one or two hours. There can be no set routine for seminarcois. As Weum stated, every parturient woman needs individual care, and it is impossible to give any definite routine to be followed in all cases. After studying a large series of cases, it is almost possible to forecast the type of narcosis obtained in a particular type of patient, even before the drug is administered.

Several other interesting observations were made while studying this series of cases. For example, in a few cases (primiparae) delivery was made by forceps and episiotomy without anesthetics because of a decompensated heart, and there were absolutely no ill effects from the administration of dilaudid-scopolamine.

Another interesting observation was made on some of the babies. Several were x-rayed on the second day of life for the purpose of determining whether or not they had an enlarged thymus gland. Some of these babies were from mothers who entered the hospital too late for seminarcois, others were included in the series. From a study of the x-ray plates in 378 cases, it was found that in 24 babies atelectasis was present although but one of these babies showed active

densed. This condensation was most pronounced in the region of the sutures. The fibrous tissue reaction was minimal. Proliferation of follicular epithelium was less marked in the smaller implants.

EXPERIMENT II

In this experiment, the left ovary of a dog was used. It was exposed and treated as in Experiment I, but the fragments were all cut small, ranging in size from 1 cm. to 0.25 cm. The number of sutures used to fix the ovarian fragments to the omentum varied from one to four. It is needless to add that some difficulty was encountered in handling the smallest fragments.

The histologic findings of these sections show functioning ovarian tissue. They all show follicles in different stages of development with the primordial phases most numerous. The number of large follicles seemed to bear a definite relation to the size of the implant and to the number of sutures used to fix the implant to the omentum. Only in the larger fragments, 0.5 to 1 cm., were Graafian follicles seen. The sections from these fragments show a moderate number of atretic follicles.



Fig. 2.—Photomicrograph of smaller implant showing a Graafian follicle in the center of the field. Atretic follicles most numerous. Adjoining omentum seen. Ovarian transplant eight months old.

In the smallest fragments, 0.25 to 0.5 cm. size, only a few atretic follicles, and some cystlike areas were noted. The fibrous tissue reaction was somewhat more marked than in the larger implants. The stroma was more condensed and the lymphocytic infiltrations seemed more numerous. This infiltration was especially pronounced in the fragments that had more than two sutures. A few giant cells were seen in the area of the sutures. The age of these implants is eight months.

Fig. 2 shows an area from the larger fragment. In the center is a Graafian follicle containing one ovum. The discus proligerus and the theca interna and externa are well defined. There are a few primordial follicles and cystic spaces in the vicinity. The adjoining omental tissue is visible.

EXPERIMENT III

The right ovary of a dog was transplanted as in Experiment I, and removed nine months later. Fig. 3 is a photomicrograph showing a typical area from the largest fragment. There are numerous follicles in all stages of development. The atretic follicles are also well represented. A portion of a corpus luteum is also included in the field. The findings resemble those in Experiment I.

fibrosis, cellular infiltration and degeneration may ensue. It was with this thought in mind that this second series of experiments was carried out. The transplants in this series were observed at the end of eight and nine months. Only autotransplants were used in this second series.

In the previous experiments done by the author, the ovary was simply bisected and then sutured to the omentum after enveloping the omentum about the transplant. In the experiments reported here varying-sized portions of ovary and a varying number of fixation sutures were used to determine the effect on the final appearance of the graft. A discussion on this point will be given below.

EXPERIMENT I

The right ovary of a dog was removed under aseptic conditions, and bisected. One half of the ovary was sutured to the adjoining margin of the omentum in



Fig. 1.—Photomicrograph of large implant showing follicles in all stages of development. Portion of corpus luteum in corner. Ovarian transplant eight months old.

such a manner that it was completely enveloped by the omentum. Long black silk sutures were used for future identification. The remaining portion of the ovary was divided into halves and one of these was again divided into equal parts. These fragments were similarly sutured to the omentum.

Transplants were removed approximately eight months later.

The histologic sections (hematoxylin-eosin stain) show functioning ovarian tissue. The photomicrograph of the larger transplants (Fig. 1) shows many Graafian follicles in all stages of development. There are also numerous primordial and atretic follicles. In this photomicrograph, there can also be seen a portion of a corpus luteum. The detail of the Graafian follicle, including the theca externa and interna, shows up clearly. The section shows only an occasional lymphocyte.

The section of the other transplants shows similar findings, i.e., functioning ovarian tissue with follicles in all stages of development, but these become less pronounced proportionately to the size of the implant. In the smallest implants, measuring approximately 0.5 cm. in diameter, the follicles were chiefly of the atretic variety with only an occasional, moderately-developed Graafian follicle. The collection of lymphocytes was more numerous and the stroma appeared more con-

the cortical tissue. The lymphocytes are not numerous in this particular section, but were found almost invariably with associated giant cells, especially where the sutures were close to each other.

SUMMARY AND CONCLUSIONS

In the preliminary paper, the results of autotransplants into the omentum were observed up to three months. The ovaries were bisected and only large portions of transplants were used. Definite evidence of functioning tissue was found in all the transplanted ovaries that were examined. The lymphocytic infiltration in the autotransplants was minimal and limited to the area surrounding the silk sutures. This was interpreted as a foreign body reaction, although no giant-cells were seen. The fibrous tissue reaction in the autotransplants was minimal. The proliferation of follicular epithelium was well marked.

In the present series, definite histologic evidence of functioning tissue was found in practically all the sections of the ovaries transplanted. The age of the implants was eight and nine months.

In this series, an attempt was made to learn if the size of the transplant or the number of sutures employed to fix the transplant would alter the final picture. It was noted that the blood vessels in the omentum in the region of the ovarian implant were essentially all of the same size. The blood supply to some of the smallest fragments which showed very little functional tissue seemed well established. (Injection studies of ovarian vessels in the transplants are being carried out, the results of which will be published in a later report.) From the results we could justifiably conclude that the two factors above did make a difference, as evidenced by the lesser number of developed Graafian follicles, the lesser amount of epithelial proliferation in the follicles, and the greater amount of fibrous tissue reaction and lymphocytic infiltration that were found in the smallest fragments, particularly in those which had the more numerous fixation sutures. This could be expressed another way; the more physical handling of the ovarian fragments, the less evidence of functioning ovarian tissue in the transplants.

When we consider the proximity of the omentum to the ovary, its striking powers for rapidly increasing its blood supply and its remarkable reaction to infectious processes, together with the experimental findings described above, we may conclude that the omentum offers an ideal site for autotransplantation of the ovary.

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EXPERIMENT IV

The left ovary of a dog was removed and divided into various-sized fragments as in Experiment II. These were attached to the omentum with a number of sutures, varying from 2 to 4. Histologic findings at the end of nine months presented an appearance essentially the same as in Experiment II. In one instance where 4 sutures had been used in a very small fragment, the omentum surrounding

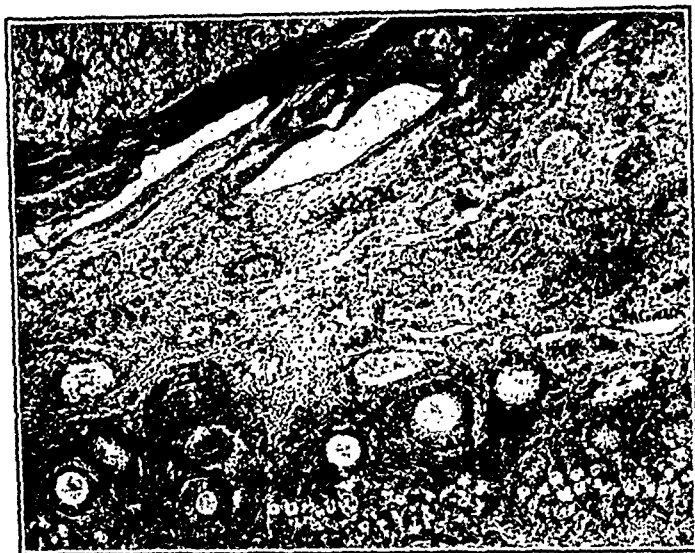


Fig. 3.—Photomicrograph showing an area from a large implant. Ovarian transplant nine months old.



Fig. 4.—Photomicrograph showing an area in a very small fragment that had been heavily sutured. One of the sutures and adjoining omentum shown. Ovarian transplant nine months old.

the implant was found adherent to the lower lateral abdominal wall. The fibrous tissue reaction was quite marked and there was relatively little proliferation of follicular epithelium.

Fig. 4 is a photomicrograph showing an area in a very small fragment that had been heavily sutured. There are a moderate number of developing follicles and a few atretic follicles adjoining the omental fat, except where the suture constricted

TABLE I. MENSTRUAL BLOOD LOSS

CASE	AGE	BLOOD			DURATION OF PERIOD DAYS	NUMBER OF NAPKINS USED	MENSTRUAL LOSS			DIAGNOSIS
		R.B.C. MILLIONS	HEMAT. %	H.B. GM.			IRON MG.	H.B. GM.	BLOOD C.C.	
1	34	4.48	31.0	6.14	2 days	4	20.57	7.14	116.28	Idiopathic hypochromic anemia
2	34	3.85	33.0	7.10	7 days	20	25.02	7.47	105.21	Menorrhagia
3	33	3.54	24.0	4.61	2 days	4	30.50	9.10	197.18	Hematuria and hypochromic anemia
4	50	4.64	35.0	10.71	3 days	6	33.75	10.07	94.02	Climacteric bleeding
5	24	4.47	34.5	9.47	8 days	16	44.80	13.37	141.21	Menorrhagia
6	40	3.63	29.0	6.20	7 days	43	47.38	14.14	228.06	Idiopathic hypochromic anemia
7	37	4.77	34.0	6.46	7 days	25	49.59	14.80	229.12	Idiopathic hypochromic anemia
8	44	4.07	28.0	6.26	5 days	21	53.42	15.94	254.31	Idiopathic hypochromic anemia
9	25	4.52	36.0	10.90	3 days	10	59.73	17.82	163.48	Idiopathic hypochromic anemia
10	42	3.97	36.0	10.22	9 days	38	95.60	28.54	279.22	Idiopathic hypochromic anemia
11	26	3.83	27.0	10.10	4 days	23	96.47	28.79	285.04	Leiomyoma
12	35	3.88	20.5	4.72	5 days	7	145.89	43.54	922.45	Menorrhagia
13	48	4.19	38.0	7.19	6 days	36	146.36	43.65	607.09	Idiopathic hypochromic anemia
14	23	3.93	32.0	7.89	22 days	65	153.69	45.87	581.37	Incomplete abortion
15	41	4.33	26.0	11.80	5 days	13	163.00	48.65	412.29	Idiopathic hypochromic anemia
16	40	4.75	38.0	12.01	5 days	20	182.07	54.36	452.42	Idiopathic hypochromic anemia
17	33	3.68	33.0	9.02	9 days	58	207.80	62.03	687.68	Fibromyoma
18	45		38.0	11.36	6 days	39	220.15	65.72	578.48	Menorrhagia

THE BLOOD LOSS IN MENORRHAGIA*

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IN ORDER to ascertain the amount of blood lost during normal menstruation, determinations were made on 100 women who were not anemic and who considered their menses to be normal in every respect.¹ The results showed a loss of from 6.66 to 178.69 c.c. of blood with an average loss of 50.55 c.c. The hemoglobin loss varied from 0.68 to 23.57 gm. with an average of 5.82 gm. It is impossible to set definite limits of normal, but the average loss for this large a series is certainly of significance.

Subsequent determinations by similar methods have been made on 18 women whose chief complaint was menorrhagia or who were admitted to the hospital with a hypochromic anemia which seemed to be due in part to an abnormal menstrual loss even though they themselves considered their menses to be normal. This brief report is merely a presentation of these findings for the purpose of recording the amount of blood and hemoglobin which is actually lost under such circumstances.

The amount of hemoglobin is the most accurate method of presentation of these data, whereas if this is expressed in terms of cubic centimeters of blood, it does not give the essential information because the results vary with the blood hemoglobin values. For example, the loss of 5 gm. of hemoglobin will represent from 33 to 100 c.c. of blood, depending on whether the patient had 15 or 5 gm. of hemoglobin per 100 c.c. of circulating blood.

METHODS

Cellulocotton pads were utilized for the collection of the menstrual flow and the material was analyzed for iron by a modification of the method of Reis and Chakmakjian.² The iron was converted to its equivalent in grams of hemoglobin, and this in turn to cubic centimeters of the patient's blood. Table I gives the essential data for each patient with their menstrual loss in terms of iron, hemoglobin, and blood. The duration of the menstrual flow and the number of napkins used are likewise recorded. Table II gives the results on 5 patients on whom more than one observation was made. We believe that all these results must be considered as abnormal since they are above the average value as determined in the preceding study, although not all are above the highest values encountered in that group.

Several cases are included in which the diagnosis of idiopathic hypochromic anemia was made. We believe this form of anemia is primarily a chronic hemorrhagic anemia occurring in a patient who is unable to properly metabolize the dietary iron.³ Most of these patients had not recognized that they were losing an abnormally large amount of menstrual blood.

*Supported in part by a grant from the Eli Lilly Co.

AN APPARATUS FOR PROCURING ESSENTIAL DATA IN THE DIFFERENTIAL DIAGNOSIS OF PELVIC PATHOLOGY IN THE FEMALE*

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DURING the past fifteen years or so in which transuterine insufflation has been increasingly used for the study of the Fallopian tubes, much has been written of its diagnostic value, its dangers, and its use as a therapeutic agent. Theoretically, at least, it would seem that this method could also be used for studies of the normal physiology, and this to some extent has been attempted.

One of the fundamental difficulties encountered in such studies has been the inaccuracy of the apparatus. Another of almost equal importance has been the discomfort to the patient resulting from the insufflation. It was in an attempt to overcome these difficulties that our first apparatus was devised.

The general structure of the apparatus can be seen in Fig. 1. It consists of: a source of gas and pressure, the smallest available tank of carbon dioxide; a graduated cylinder and plunger to contain the gas used during the procedure, above which is a pressure reservoir by which the plunger may be forced into the cylinder; a mercury manometer for the gross measurement of pressure which is connected, by means of a float and stylus, for the recording and accurate measuring of pressure; an exhaust valve for immediately exhausting the entire system; a safety valve to maintain a given predetermined pressure in the entire system, adjustable from zero to 220 mm.

In operating the apparatus the safety valve is first adjusted by elevating or lowering the mercury container, in which rests the tube connected to the gas line between its source, the tank, and the remainder of the apparatus. This pressure on the first examination should obviously not exceed the normal pressure, 100 to 120 mm., subsequent pressures to be determined by the findings on the first examination. The valve of the gas tank is then opened, the flow being roughly controlled by a needle valve, to supply a constant stream of bubbles through the mercury safety valve. The gas is then turned into the graduated cylinder filling it to the required volume, which our experience so far has shown us to not exceed 25 c.c. By now shunting

*A paper on the clinical value of the uterosalpingogram ("The Utero-Salpingogram as a Means of Differential Diagnosis in Gynecological Pathology." J. Med. Cincinnati, Ohio, Nov., 1936.) was followed by many requests for an explanation of the technique and apparatus used. Before discussing this, however, I should like to express my appreciation for the invaluable cooperation of Dr. T. J. LeBlanc, Professor of Preventive Medicine, in the development of the original equipment and of the work of W. E. Stilwell, Jr., in the building of our present apparatus, and to Drs. H. G. Reincke, William Doughty, and E. R. Bader, Department of Radiology, for their assistance in the x-ray phase of the study.

RESULTS

The hemoglobin lost per menstrual period in these 18 cases varied from 7.14 to 65.72 gm. This represented a loss of from 94.02 to 922.45 c.c. of the patient's blood, as calculated from their actual blood hemoglobin. The degree of anemia did not parallel the amount of blood lost.

TABLE II. VARIATIONS IN THE MENSTRUAL BLOOD LOSS IN THE SAME INDIVIDUAL

CASE	AGE	BLOOD			MENSTRUAL LOSS			DIAGNOSIS
		R. B. C. MILLIONS	HEMAT. %	HB. GM.	IRON MG.	HB. GM.	BLOOD C.C.	
5	24	4.73	36.0	10.73	38.00	11.34	105.71	Menorrhagia
		4.47	34.5	9.47	44.80	13.37	141.21	
10	42	4.52	36.0	11.29	78.40	23.40	207.28	Leiomyoma
		3.97	36.0	10.22	95.60	28.54	279.22	
15	41	4.44	41.0	12.63	100.40	29.97	237.39	Idiopathic hypochromic anemia
		4.33	26.0	11.80	163.00	48.65	412.29	
16	41	4.15	33.0	7.36	50.62	15.11	205.15	Idiopathic hypochromic anemia
		4.75	38.0	12.01	182.07	54.36	452.42	
18	46	3.79	31.5	7.71	186.29	55.61	720.79	Menorrhagia
			38.0	11.36	220.15	65.72	578.48	

In Table II are presented those cases in which more than one observation was made. These are numbered to correspond to their position in the preceding table in which the period with the greater loss is given. It will be noted in Cases 5 and 10 that the variation was not great, whereas in the other 3 cases, and particularly in Case 16, there is a great variation from one period to the other.

We have been unable to find reports of a similar nature in the literature except that of Hoppe-Seyler⁴ who analyzed the menstrual loss in 15 women. In 4 normal cases the average loss was 37 c.c. of blood, while in the 11 abnormal ones the loss ranged upward to 376 c.c.

COMMENT

Although no very definite limits of the normal menstrual blood loss can be set, we present these results as representative of abnormal menstruation. Not all of the patients appreciated the fact that their periods were more profuse than the average. Even the patient (Case 12) who lost 43.54 gm. of hemoglobin, or 922.45 c.c. of blood, stated that her menses were not profuse. Since these individuals have no means of comparison, it is obvious that one cannot rely on their statement as to the normalcy of their menses.

No definite conclusions can be drawn from these results as to the amount of blood lost in individual cases of menorrhagia, and the data are presented merely as accurate measurements in certain pathologic cases.

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From the 2,783 insufflations for which this apparatus has so far been used, we draw the following observations. Though there may be occasional discomfort in the region of an opening tube, it is of short duration, relieved by exhausting the apparatus, and it is very seldom followed by subphrenic referred pain, which, though of diagnostic value,

100

CASE #102

JAN. 20, 1932

23 DAY OF MENSTRUAL CYCLE

START 150 CC. ATM.

" 110 CC PRESS

" 100 CC SYSTEM FULL

USED 10 CC. INTERNALLY

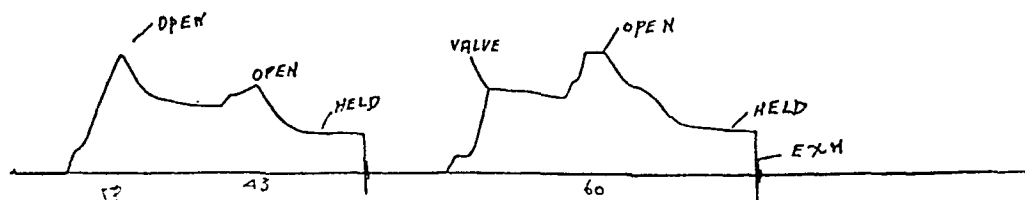


Fig. 2.—Normal graph showing the relatively sharp opening, fall in pressure, and gradual reduction.

Case 172

Oct 21 1932

Start 40

High 10

Used 20

Cycle 12

Pen R trap pp by alt L trap.

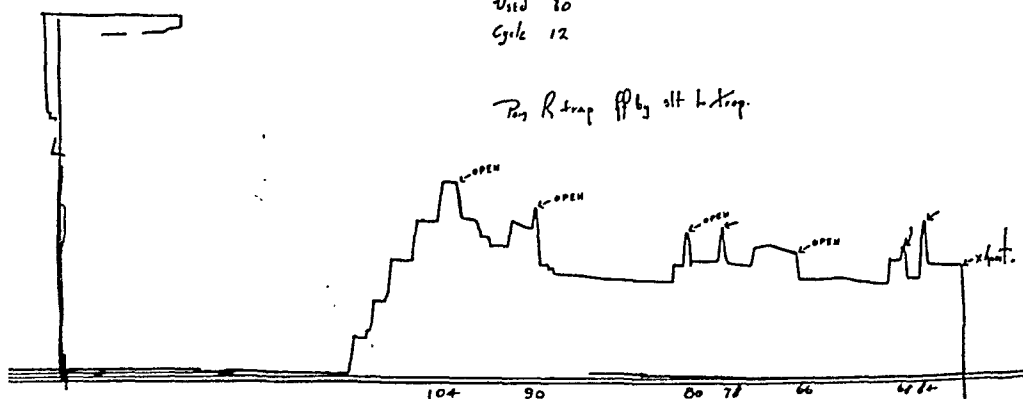


Fig. 3.—Dysmenorrhea showing the spasmodic response, gradual reduction over all by frequent marked elevations followed immediately by an acute fall, the average remaining normal or high.

is not necessary. It has not been necessary for patients to rest following the insufflation, since they are able to continue their activities immediately. The recording apparatus, as checked against an independent manometer, has an inaccuracy never to exceed 1 mm. in 200. The volume required has so far never exceeded 25 c.c., even when repeated checks have been made at one sitting and can be read or estimated within 1 c.c.

the gas into the pressure chamber above the plunger, a pressure can be exerted upon the gas in the cylinder equal to, but never exceeding, the pressure at which the mercury safety valve has been set. When it is desired to insufflate, the needle control valve between the graduated cylinder and the manometer is slowly opened, allow-

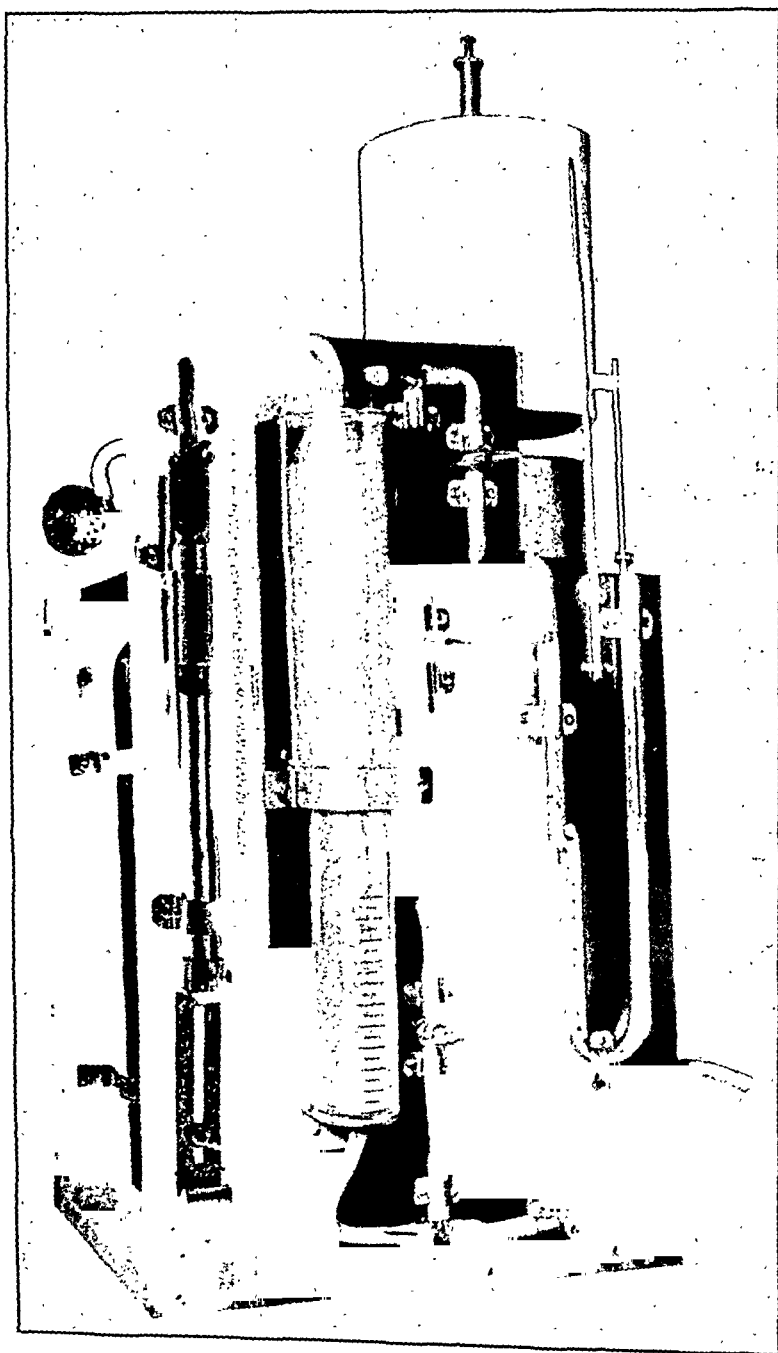


Fig. 1.—Original apparatus.

ing the gas to escape through the tube into the uterine cannula; the manometer and recording apparatus, being shunted in parallel with this side of the system, will fluctuate with any changes in pressure. When the desired results have been obtained, the exhaust valve is turned, exhausting the uterine side of the apparatus instantaneously.

highest pressure; (2) the patient and the apparatus are automatically disconnected (a) when the reservoir pressure approaches zero, (b) when the pressure within the patient is reduced as a result of opening of the tube, leakage, etc., and (c) when the pressure within the patient has reached a predetermined maximum; (3) a graphic record is made which is accurately synchronized as to time and pressure for gas and oil; (4) it contains a maximum pressure regulator, adjustable from zero to 300 mm.; (5) the lighting of the dials is so arranged as to permit dimming below the point of objection for use during fluoroscopy, still allowing visibility; during the use of the apparatus the red and green lights are a constant indicator to the operator as to whether the patient is or is not connected; (6) remote control—the entire control of the apparatus is by means of a single hand switch on a cord of any length convenient, thus permitting the operator to be at any distance from

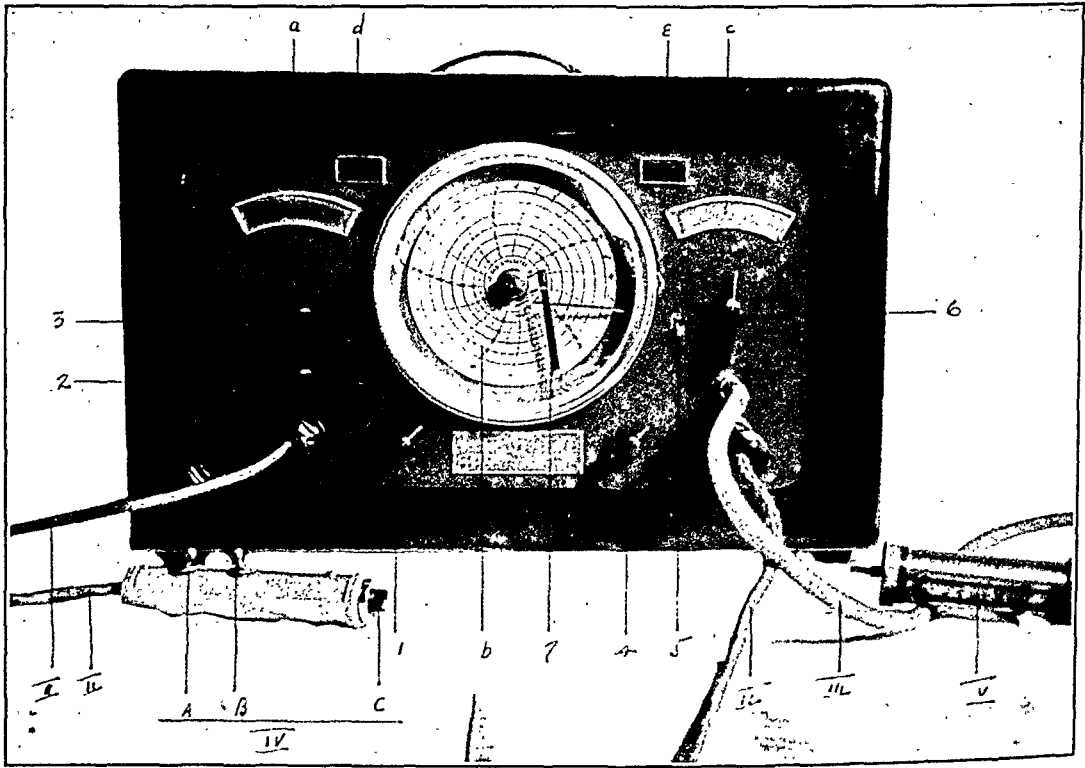


Fig. 5.—Front view of apparatus.

the apparatus during manipulations within the patient; (7) the oil reservoir permitting the instillation of opaque oil under the controlled gas pressure of the apparatus with a graphic record; (8) a gas filter; (9) an attachment permitting the use of compressed gasses, this is attached at the head of the gas filter as a lead to the tank of compressed gas, if such a tank is used it must be equipped with a reducing valve; (10) built so compactly as to be portable.

In Fig. 5 is shown the control panel: *a*, finger dial indicator of the gas pressure within the reservoir; *b*, a rotating chart dial graphically representing time and pressure connected, as later described, for the automatic cut-out at reduced intra-uterine pressure or maximum pressure; *c*, a finger indicator dial for maximum pressure, adjustable from 0 to 300 mm.; *d*, green light; *e*, red light; *1*, the switch to turn on current from wall plug; *2* and *3*, switches to control intensity of illumination of dials; *4*, switch controlling the rotation of the graphic chart, *b*; *5*, adjust-

The exhaust requires by stop watch timing two seconds to evacuate the uterine side of the apparatus, a slight negative pressure being produced which probably accounts for the immediate cessation of symptoms.

The accompanying graphs (Figs. 2, 3, and 4) illustrate a few of the changes occurring both in apparently normal and in abnormal tubes with reference to phases in the menstrual cycle, dysmenorrhea, etc. The group is not sufficiently large, as the majority have been sterility cases, to permit of analysis, certainly not of conclusions at the present time, but is constantly increasing. It will also be noted that the apparatus is extremely sensitive and extraneous influences must be carefully controlled by the operator. It has also been found that due to the ease

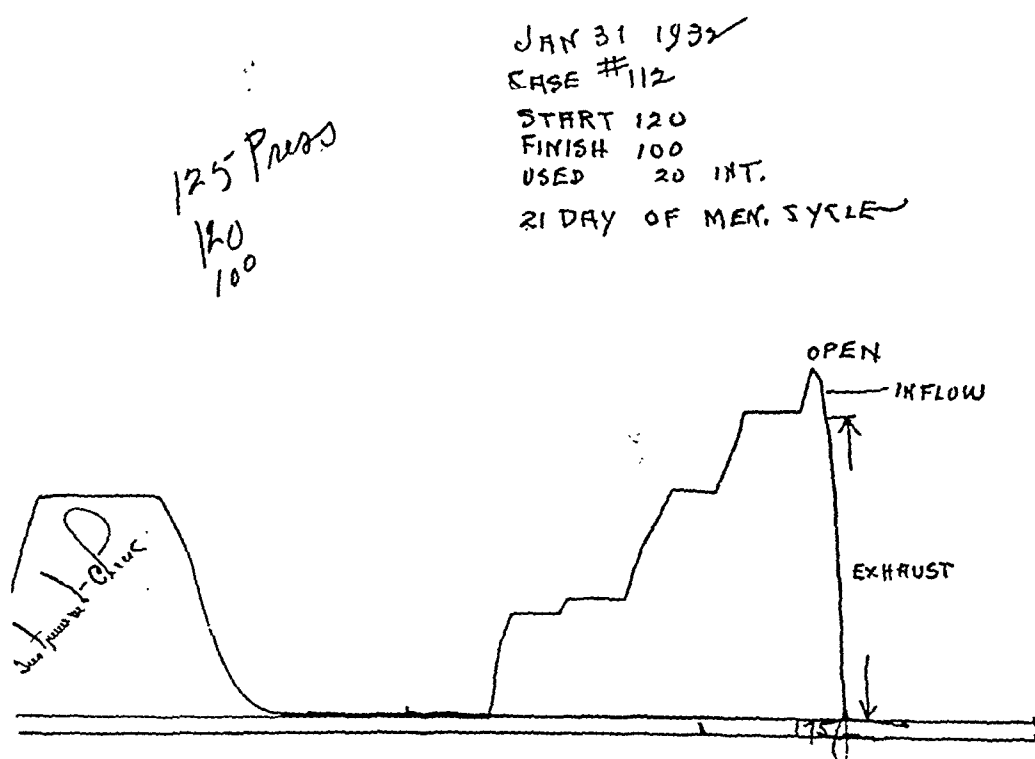


Fig. 4.—Partial tubal obstruction: a rather typical picture of the strictured or partially occluded tube, opened by gradually increased pressure and volume as the steps on the curve show. (Sterility due to mechanical obstruction successfully relieved by repeated dilatation by insufflation.)

of control and adaptability of the apparatus, an entire set of graphs can be made and checked in fifteen minutes or less with no discomfort to the patient.

Since the above described apparatus was completed (1931) and very satisfactorily used in well over a thousand cases, an apparatus was constructed, working on the same principles, but so controlled electrically as to be automatic, compact, and include a method of injecting opaque oil.

It includes the following features described in detail below: (1) gas pressure starts from zero and is gradually increased rather than being reduced from the

valve and cannula, a "disconnect" occurs, the red light goes off and the green light comes on. If the latter occurs, the switch is again thrown, this time for a longer period. This flow of gas can also be noted on the recording chart, since the stylus will gradually rise as the gas increases the intrauterine pressure. The procedure is continued by running the compressor sufficiently to maintain a gas pressure in the reservoir as indicated on dial *a* in Fig. 5. Under ordinary circumstances for insufflation, a reservoir pressure of around 200 mm. is more than adequate. Dial *a* indicates *only* the pressure in the reservoir and has no significance as to the intra-uterine pressure which is indicated on chart *b* only.

When gas escapes from either or both of the Fallopian tubes, or when the maximum pressure, previously adjusted on dial *c*, Fig. 5, is reached, the apparatus is

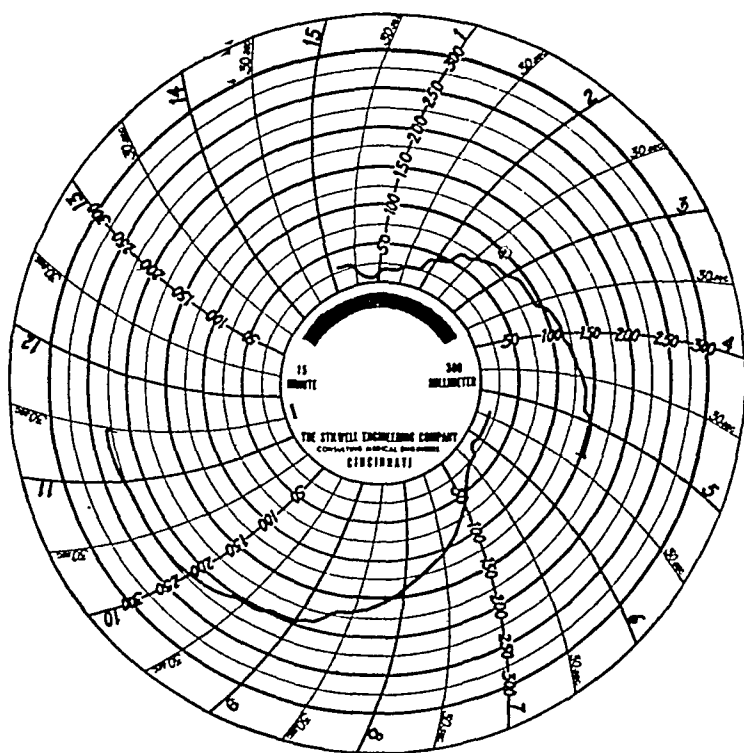


Fig. 7.

automatically disconnected from the patient, as explained above. Leakage around the cannula, of course, is noted by bubbling through the "water seal," by a "disconnect," or by both.

When an x-ray examination with opaque media is to be done, the procedure is the same as outlined above, except that the oil cartridge *V* is inserted between the uterine cannula and the end of the flexible tube, and the maximum pressure control is raised 150 mm. above insufflation opening. (This is the approximate oil resistance. This figure can be obtained in any given instance by determining at what pressure oil starts flowing through the cannula before its insertion into the uterus.) The gas pressure is then gradually increased, as with insufflation, the oil noted under the fluoroscope as it enters the uterus and tubes, and films made as indicated. This fluoroscopy and films can then be checked with the graphic record on the chart.

Our usual procedure is to do an insufflation and immediately follow it with x-ray without moving the patient from the table, since the roentgenologic findings

ment lever for stylus, 7; 6, knob for adjusting maximum pressure control: *I*, Lead from source of electrical supply; *II*, remote control lead; *III*, tube leading to cannula within the patient with male and female Luer fittings; *IV*, hand control (remote control)—*A*, switch for manually disconnecting apparatus from patient by operating the mechanism controlling valve in the line to the patient; *B*, switch for operating contact mechanism; *C*, button controlling operation of motor-compressor unit; *F*, oil reservoir-cartridge for instillation of opaque oil.

Fig. 6 is a view of the apparatus with the back of the cabinet removed.

PROCEDURE

The uterine cannula is placed in or through the cervix with the usual technique for insufflations, using surgical care for antisepsis. The patient is then placed in a slight Trendelenburg position and the vagina filled with a mild antiseptic solution

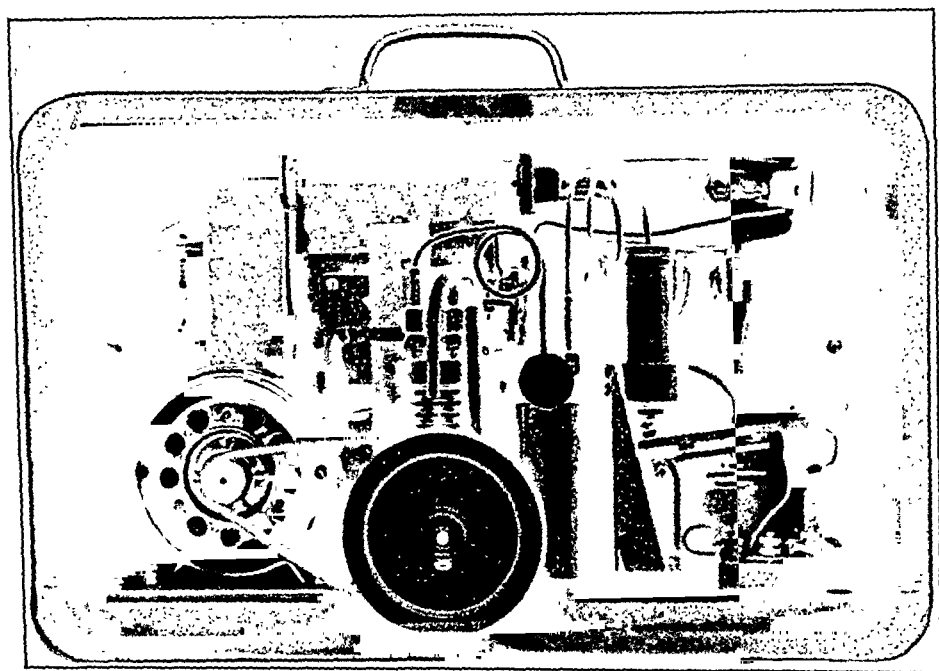


Fig. 6.—Rear view of apparatus.

making a "water seal"; the cannula is connected with the apparatus by means of the flexible gas tube with Luer fittings (Fig. 5, *III*); switch 1, Fig. 5, is turned for a current supply; switches 2 and 3 are turned as needed for the control of the light intensity on the dials; switch 4, Fig. 5, is turned to start the recording chart *b*, Fig. 5, rotating; lever 5, Fig. 5, is adjusted so the stylus 7 makes a tracing on the chart; switch 6 is turned to set the indicator at the maximum pressure beyond which it is not desired to have the apparatus operating at a given time.

By pressure on the button of the remote control *IV*, *C*, Fig. 5, the motor-compressor starts operating, building a reserve pressure in reservoir indicated on dial *a*, Fig. 5. The switch *IV*, *B*, on the remote control is then turned making contact through the mechanism regulated by the stylus arm operating the control valve in the line to the patient. At this point the green light *d* goes off and the red light *e* comes on. When the gas has started flowing through the cannula, the remote control switch *IV*, *B* is turned to its original position and the red light continues glowing; however, if this switch is thrown before gas is actually flowing through the

2. The synchronization of the contact and control mechanism with the hand switch has a sufficient latent period to make it impossible to start a flow of gas without conscientious concentration on the part of the operator.

3. The hand control permits free movement of the operator at any convenient distance from the apparatus with absolute control of the apparatus, even to immediate disconnection if indicated.

4. The flow of gas and oil is so sufficiently slow and regular that the patient has no subjective symptoms other than an occasional sensation of fullness and is able to be up and about immediately following the manipulation.

5. By *deliberately* setting the various control switches, it is possible, if desired, to continue the flow of gas or oil ad lib. if a pneumoperitoneum, etc., is desired. (Note the emphasis on deliberate.)

6. The data obtained from the use of this apparatus, gas pressure, x-ray, etc., we have found of great value in the differential diagnosis of female pelvic pathology by no means limited to the study of the problem of sterility.

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Haselhorst, G.: A Single Mishap in Tubal Sterilization in the Female, Zentralbl. f. Gynäk. 61: 306, 1937.

Haselhorst has employed the method of crushing the Fallopian tubes in 170 women as a means of sterilization. Thirty-five of them were subsequently investigated radiologically; one woman had one patent Fallopian tube. He has found this method simple and effective on nonpregnant women but definitely unreliable when it is combined with evacuation of a pregnant uterus, or for the treatment of a patient during the puerperium. The writer contradicts the suggestion made by Hartmann, that he only aims at the destruction of the peristaltic tubal action without obliteration of the lumen. He considers it essential to destroy the whole tubal wall except the peritoneum when crushing the tube.

J. P. GREENHILL.

are of paramount importance, and unless contraindicated, should always be done for diagnoses, although not always necessary in follow-up therapy.

The graphic chart (Fig. 7) shows the curve of increase in transuterine pressure with gas, with its abrupt fall when the tube opens; followed by a curve of the gradually increasing pressure during the oil instillation for fluoroscopy and x-ray. Note that the chart records the time factor of flow, as well as pressure, and from these can be computed the relative gas volume used.

The x-ray plate of the uterosalpingogram corresponding with the chart curve of Fig. 7 is shown in Fig. 8. A comparison of these two with timing permits the interpretation of the rate of flow, etc., from which the diagnoses are made.

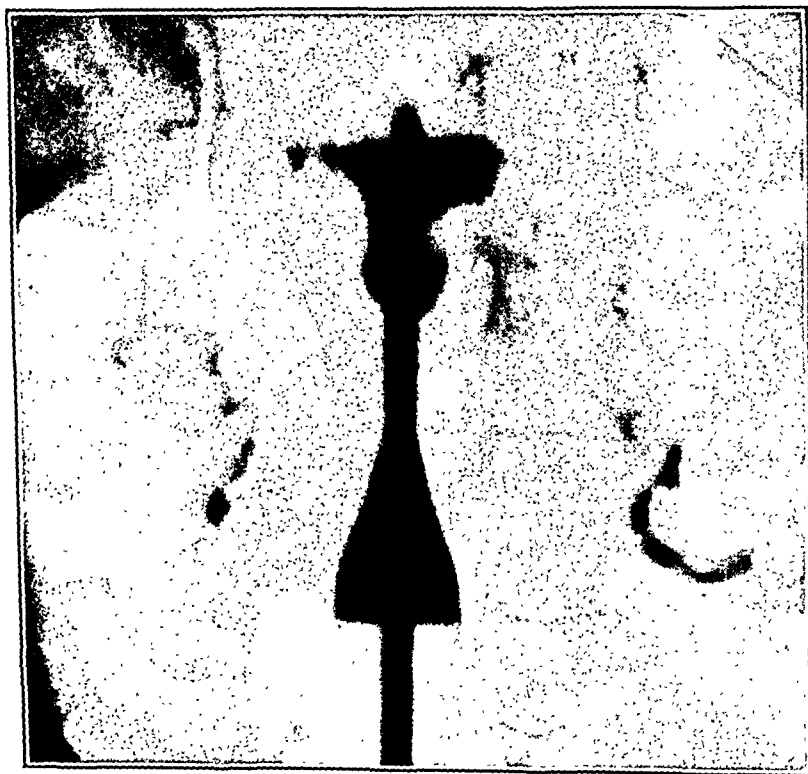


Fig. 8.—Uterosalingogram of patient shown in curve of Fig. 7.

SUMMARY

An apparatus has been developed which permits of an automatic control of the maximum pressure of gas within the uterus with automatic safety factors well within the danger limit. This apparatus also permits of controlled instillation of opaque oils for x-ray study of pelvic pathology. These procedures are regulated by a simple hand-switch carried by the operator. The apparatus produces an accurate graphic record of time and pressure both of gas and oil.

CONCLUSIONS

Reviewing 393 examinations for which the latter apparatus has been used, the following tentative conclusions have been drawn:

1. The disconnect apparatus, being electrically controlled, is practically instantaneous in its response.

tion of the fetal thorax with reference to the mother's abdominal wall; and (4) the presence of adventitious sounds. Furthermore, just prior to actual delivery the accoucheur is frequently dependent for the interpretation of the fetal heart sounds upon an assistant or nurse who may encounter delay in locating them, and in so doing may cause dishevelment of the sterile drapes. This may be especially annoying with a distraught or difficult patient.

To obviate some of these undesirable features and conditions, the thought occurred to us that with modern electrical equipment one might be able to amplify the fetal heart tones with an intensity and fidelity heretofore difficult to obtain. The use of the vacuum tube amplifier in connection with the auscultation of clinical sounds is not new.

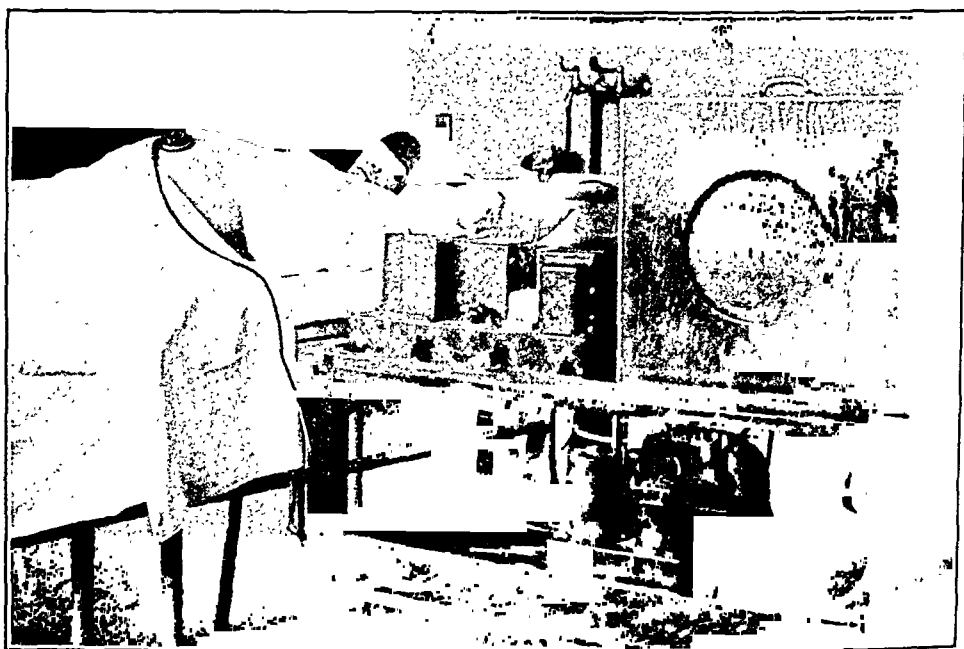


Fig. 1.—Photograph showing the apparatus in operation. The portable feature allows the amplifier to be placed in an adjacent room.

Squier¹⁰ in 1921 demonstrated the practicability of amplifying the adult heart sounds with such a method. Abbott¹¹ in 1922 described an amplifying device that enabled hundreds of persons in a large room to hear the heart sounds with the aid of a loud speaker, and according to Keiper,¹² a similar device has been used to demonstrate the fetal heart sounds. Jacobsohn¹³ suggested the use of the vacuum tube in obstetrics. Gamble and Replogle¹⁴ were able to reproduce fetal heart sounds on a loud speaker by means of a mechanism described by them and by Cabot.¹⁵

In our opinion, the potential value of a device for the amplification of the fetal heart sounds has not been generally appreciated nor sufficiently emphasized. That this is true is not surprising when one considers that heretofore, and for the most part, suitable equipment has been costly, bulky, and cumbersome. Likewise, for years technical difficulties made reception of sounds unsatisfactory. More recent develop-

AMPLIFICATION OF FETAL HEART SOUNDS*

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THE ability to perceive fetal heart sounds provides impeccable evidence not only of pregnancy but also of fetal life. Auscultation, moreover, furnishes confirmatory evidence concerning the presentation and position of the fetus, and may be helpful in the detection of a multiple pregnancy. More important, it provides one of the few reliable means of recognizing impending peril to the life of the fetus, as during a prolonged and difficult labor, or one which is associated with hemorrhage. Its usefulness is apparent in the diagnosing of a suspected stillbirth. One will not infrequently be called upon to select a mode of delivery when the prudent decision will be dependent upon the establishment beyond peradventure of the well being or death of the fetus. Lack of exact information on this point may lead to tragic diagnostic error. The characteristics of the fetal heart sounds may foretell threatening asphyxia and demand immediate operative delivery by means of which an otherwise hopelessly doomed child may be rescued. Seldom indeed would one be required to do a destructive operation on a living child. Moreover, when death of the fetus is once recognized, advised conservative care of the mother becomes the only important consideration; and her interests may often then best be served if deliberation supplants haste.

Whereas Fasbender¹ ascribes the first audition of fetal heart sounds to LeGoust in 1650, others^{2, 3} record that these sounds were first heard by Mayor⁴ of Geneva in 1818. This was two years after Laennec's⁵ discovery of the stethoscope. Unaware of Mayor's disclosure, Kegaradec⁶ in 1822 also heard the sounds of the fetal heart and described these in his classical monograph with such completeness that many years passed before significant additions were made to his accounts. DePaul,⁷ who claimed to have heard the fetal heart during the eleventh week of uterogestation, in 1847 suggested auscultation as an aid in determining the position of the fetus. In 1907 Einthoven⁸ applied the capillary electrometer as a means of registering and analyzing heart sounds. Williams⁹ in 1921 converted sound oscillations into electrical oscillations by means of an electromagnetic transmitter and used a string galvanometer to graphically record heart murmurs.

Unfortunately, the fetal heart sounds are infrequently audible before the sixteenth to twentieth week of pregnancy. Even after this time, adverse conditions may render satisfactory auscultation difficult. Among these conditions may be cited: (1) An obese abdominal wall; (2) an excessive amount of amniotic fluid; (3) an unfavorable posi-

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the usual methods of examination. After following the vagaries of a given fetal heart during the time preceding delivery, one learns what to expect by way of variations and may thus eliminate one source of anxiety.

Although we have applied this equipment only to a comparatively small series of normal cases, we believe that its practical utility in diagnosis is apparent. The ease with which the microphone can be retained in position facilitates repeated examination and precludes the inconvenience of a disturbing feature concerned with repeated exposure of the patient. And if a prediction is allowable, we believe that this general method will prove useful in gaining further information relating to physiologic and pharmacologic influences on the fetal heart.

We wish to acknowledge the technical assistance and cooperation rendered by Dr. Ray Manson, Mr. Fred Young, and Mr. Oliver Angevine. The equipment was provided by the Stromberg Carlson Telephone Manufacturing Co.

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For completing a miscarriage the curette is not dangerous provided the cervix has been adequately dilated and the principal mass is removed with a large blunt curette. Prophylactic immunization with Streptoserin was found very valuable in cases of infected abortions.

In cases of habitual abortion, Proluton is injected weekly after the sixth week for a period of 4 to 5 months.

A diet during pregnancy, especially during the last two months, which includes very little milk and practically no meat tends to prevent oversized babies and more serious metabolic disturbances.

Wolff recommends bag induction of premature labor.

Walcher's position furthers entrance of the fetal head into the inlet, especially in the case of a flat rachitic pelvis.

The parturient's position, especially on the side, influences rotation and causes a particular portion of the head to descend lower.

C. E. PROSHEK.

ments of the radio arts have produced small and relatively inexpensive high gain AC operated amplifiers with a very low hum level and large power output. Such an outfit was made available to us, and upon actual test we were able with it to hear the fetal heart sounds with good room volume, clarity, and freedom from many of the distortions and difficulties that had previously beset efforts to satisfactorily amplify the sounds.

DESCRIPTION OF APPARATUS

The amplifying equipment consists of a stock Stromberg-Carlson AC operated 11-A amplifier in conjunction with their No. 13 Universal amplifier. This combination has a total gain of 108 decibels with a frequency response flat with less than 3 DB total variation from 30 to 10,000 cycles per second. The amplifier is capable of 12½

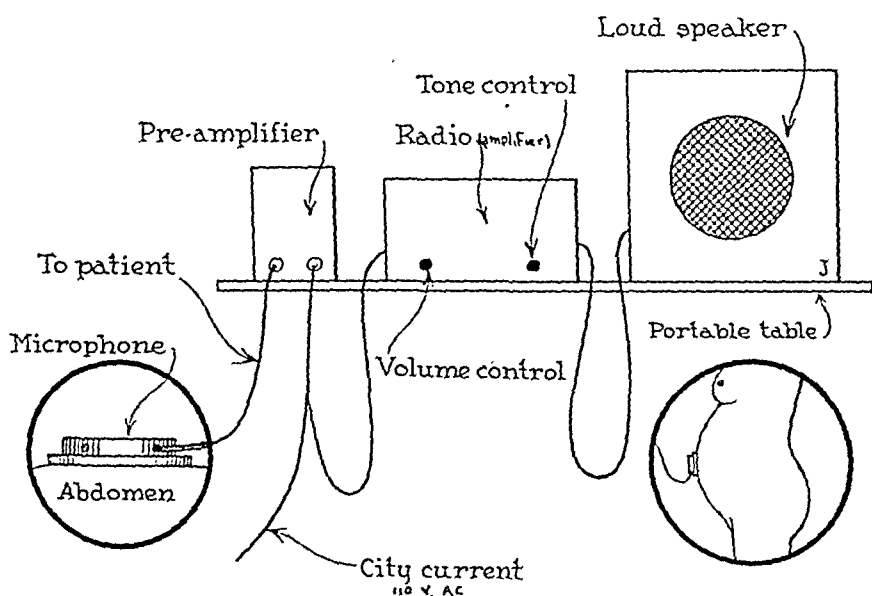


Fig. 2.—Schematic diagram of apparatus.

watts output or +33.2 DB when zero level is taken as 0.006 watts, with less than 5 per cent harmonics. The hum level is at least 50 DB below maximum output. A modified earphone of an impedance to match the preamplifier serves as the microphone or pick-up, and is placed over the point of maximal impulse of the fetal heart. The diaphragm has been made free floating to improve the low frequency response. The labor and delivery rooms are all acoustically treated and permit the use of the loud speaker in the same room as the microphone, at fairly high volume levels, without acoustic feedback. We have been able to obtain sufficient output from the amplifier, with the fetal heart sounds, to cut satisfactory phonograph discs, using the new acetate records common in electrical transcriptions for radio purposes.

This recording equipment is being used as a means of preserving the heart sounds in unusual cases and to build up a library of discs for teaching purposes, and will be described in another paper. It is hoped that these devices will aid in clinical instruction. Since the fetal pulse is very labile, continuous auscultation of the heart gives much more accurate information of the true state of affairs than is possible with

The following six cases may serve as typical of the reactions of each of the corresponding groups, respectively:

Group I.—Blood pressure 144/100. B. S., aged nineteen years, para 0, admitted not in labor May 13, 1937; referred to hospital by Welfare Clinic because of severe headaches, edema of face, eyes, and lower extremities, and albuminuria of several weeks' duration; albumin plus 4, sedimentation 30 mm. in fifty minutes, eye grounds negative, Wassermann negative, nembutal capsules one q.i.d.

5/13/37—Patient admitted

5/14/37—Blood pressure 146/100

5/15/37—Blood pressure 170/120, three capsules q.i.d. as pressure progressed into Group IV

5/17/37—Blood pressure 170/120, labor set in and delivery of premature (seven months) live infant; following delivery, pressure dropped to 130/100

5/18/37—Blood pressure 137/70, nembutal discontinued, edema gone, high colonic irrigations once daily with low protein diet

5/20/37—Blood pressure 126/88

5/22/37—Blood pressure 118/70

5/24/37—Blood pressure 118/78

5/25/37—Blood pressure normal, sedimentation 15 mm. in one hour, patient discharged in good condition

GROUP II.—Blood pressure 150/100. B. T., aged sixteen years, para 0, admitted to hospital May 6, 1937, not in labor. Complained of occasional headaches and edema of eyelids, albumin plus 2, sedimentation 33 mm. in 25 minutes, eye grounds negative, nembutal capsules two t.i.d.

5/ 6/37—Patient admitted

5/ 7/37—Blood pressure 154/100

5/ 8/37—Blood pressure 140/90

5/ 9/37—Blood pressure 138/90, edema gone

5/10/37—Blood pressure 140/90, labor began

5/12/37—Blood pressure 130/90, delivered full-term live infant, nembutal discontinued

5/14/37—Blood pressure 110/60

5/15/37—Blood pressure 104/68, albumin negative

5/18/37—Blood pressure 100/60, patient discharged in good condition

Group III.—Blood pressure 166/128. I. F., aged nineteen years, para 0, admitted not in labor Feb. 24, 1936, from prenatal clinic because of rising blood, pressure, severe headaches and impaired vision, albumin negative, sedimentation 28 mm. in one hour, eye grounds negative. Wassermann plus 4, phenolsulphonephthalein 55 per cent in two hours, blood urea clearance 58 per cent (Cs), nembutal capsules two b.i.d.

2/24/36—Patient admitted

2/25/36—Blood pressure 188/144, two capsules t.i.d. as pressure is rising

CORRELATION BETWEEN BLOOD PRESSURE AND NEMBUTAL DOSAGE IN THE TOXEMIAS OF LATE PREGNANCY

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HIGH blood pressure (140 systolic or above) is generally the first and most reliable clinical finding to signify the advent of the toxemias after the twentieth week. Similarly a high and rising blood pressure indicates increasing toxemia which if not checked may terminate in convulsions, uteroplacental apoplexy, cerebral hemorrhage, or death; all obstetric calamities.

In this report is presented a dosimetric schedule based on the height of the blood pressure, using nembutal as our basic therapeutic agent.

METHOD

The following plan was devised. Our cases were divided into 6 groups according to the blood pressure heights and treated with nembutal, put up in $1\frac{1}{2}$ gr. (90 mg.) capsules, in graded doses per os:

Group I, with blood pressure of 140 to 149, received 1 capsule q.i.d.

Group II, with blood pressure of 150 to 159, 2 capsules, t.i.d.

Group III, with blood pressure of 160 to 169, 3 capsules, t.i.d.

Group IV, with blood pressure of 170 to 179, 3 capsules, q.i.d.

Group V, with blood pressure of 180 to 189, 3 capsules 4 to 5 times daily.

Group VI, 190 and above, venesection plus 2 to 3 capsules 3 to 4 times daily.

The standard dosages were modified subject to individual responses within each group (see type cases). The prevalent measures of combating pregnancy toxemias were used concurrently with this dosimetric method.

Sixty cases of late pregnancy toxemias in our series during the past two years were treated in accordance with the above schedule and not one developed any of the above obstetric calamities. In the selection of our cases, those with preexisting hyperpiesis and/or chronic glomerulonephritis were not included.

- 8/31/36—Blood pressure 176/106, delivered a stillborn fetus, albumin 3 plus
9/ 1/36—Blood pressure 118/102, nembutal stopped
9/ 5/36—Blood pressure 118/102
9/13/36—Blood pressure 120/90, Fouchet 14 mm. in one hour, albumin plus 2, patient discharged in good condition

GROUP VI.—Blood pressure 190/130. A. P., aged sixteen years, para 0, admitted June 17, 1936, complaining of shortness of breath, dizziness, edema of ankles, albumin plus 4, eye grounds negative, Fouchet negative, nembutal capsules one t.i.d. until delivery June 19, and 5 capsules during delivery, then discontinued, all contrary to orders.

- 6/17/36—Patient admitted
6/18/36—Blood pressure 172/120
6/19/36—Blood pressure 206/140, delivered full-term live infant
6/20/36—Blood pressure 186/106
6/22/36—Blood pressure 248/128, 2 convulsions, albumin one-plus, nembutal 2 capsules intravenously and 8 capsules per os. The dosimetric schedule started. No further convulsions which in the first place might have been prevented had the treatment plan been instituted from the beginning and followed through
6/23/36—Blood pressure 210/122
6/24/36—Blood pressure 186/120
6/25/36—Blood pressure 172/116
6/26/36—Blood pressure 155/110
6/27/36—Blood pressure 144/96
6/28/36—Blood pressure 140/100
6/29/36—Blood pressure 135/90
6/30/36—Blood pressure 130/85, patient discharged in good condition

This case was especially selected from its group to emphasize the importance of rigorous adherence to the method advocated in order to make certain the eliciting of the anticipated results.

DISCUSSION

From the study on these cases of the correlative action of nembutal and response of the high blood pressure in the treatment of the late pregnancy toxemias, we are led to believe that a high and rising blood pressure is a reliable index of the degree of the toxemia. The high blood pressure was markedly reduced towards normal following the use of nembutal (Ross¹) and amelioration of other symptoms of the toxemia synchronized the reduction of the blood pressure.

The satisfactory results obtained from the use of nembutal by the above dosimetric plan have convinced us that the procedure is rational and worthy of recommendation.

- 2/27/36—Blood pressure 166/134
2/28/36—Blood pressure 164/130
2/29/36—Blood pressure 162/126, 158/120
3/ 1/36—Blood pressure 158/122
3/ 4/36—Blood pressure 150/118
3/ 7/36—Blood pressure 188/130, labor set in, albumin plus 4, hyaline and granular casts and pus cells
3/ 8/36—Blood pressure 210/132, and delivery of premature live infant
3/ 9/36—Blood pressure 180/120
3/11/36—Blood pressure 154/110
3/12/36—Blood pressure 138/100
3/14/36—Blood pressure 128/92, nembutal discontinued
3/16/36—Blood pressure 124/80
3/19/36—Blood pressure 120/80, patient discharged in good condition

This case did not receive the full scheduled dosage of nembutal as anti-syphilitic treatment was given concurrently; however, there was a gradual decline in blood pressure to normal.

GROUP IV.—Blood pressure 170/100. M. D., aged thirty-one years, para 0, admitted in labor Aug. 9, 1936, with edema of legs and delusions of design on her life by her people and persecution, albumin plus 4, sedimentation 32 mm. in one hour, eye grounds negative, Wassermann negative, Fouchet test positive in 5 min., phenolsulphonephthalein 55 per cent total output, nembutal given as per schedule.

- 8/ 9/36—Patient admitted; 2 hours after admission pressure 192/112; 5 hours after admission blood pressure 210/100; venesection of 500 c.c. of blood plus scheduled use of nembutal

8/10/36—Delivered stillborn infant at term

8/11/36—Blood pressure 165/100

8/13/36—Blood pressure 152/94, edema gone

8/16/36—Blood pressure 122/84, nembutal discontinued

8/20/36—Blood pressure 100/80

9/ 7/36—Sedimentation 13 mm. in one hour

9/ 8/36—Mentally clear

9/11/36—Fouchet test negative

9/20/36—Blood pressure 105/75, patient discharged in good condition

GROUP V.—Blood pressure 184/100. E. R., aged thirty-six years, para 0, admitted Aug. 24, 1936, having had 4 convulsions, albumin plus 4, sedimentation 26 mm. in one hour, eye grounds negative, Wassermann plus 4, edema of face, hands and feet, mental confusions, phenolsulphonephthalein 65 per cent total output, nembutal given per schedule. No further convulsions.

8/24/36—Patient admitted

8/26/36—Blood pressure 136/98, mentality clear

8/28/36—Blood pressure 140/86

8/30/36—Blood pressure 166/100, in labor, edema gone

Wellcome in the form of ergometrine; and Sandoz in the form of basergin.*

Davis, Adair and Pearl⁸ using ergonovine malleate (ergotrate, Lilly) concluded that their cases exhibited an increased rate of involution and a lessened morbidity. Beecham⁹ using ergostetrine (ergoklonin, Wyeth) also found an absence of subinvolution. DerBrucke¹⁰ using ergostetrine (ergoklonin, Wyeth) found a too tonic action of this oxytocic giving sapremic temperatures.

PROCEDURE

As control cases 50 patients received no oxytocic medication during their stay in the hospital. The height of the fundus was measured daily as an indication of the involution of the uterus and a note was made as to the amount of bleeding and subjective symptoms of the patient. The next 400 consecutive deliveries were divided into groups of 100. The patients in each group were given one of the following medications immediately after the delivery of the placenta: (a) ergotrate (Lilly) 0.2 mg. intravenously (Kharasch and Legault's ergotocin); (b) ergoklonin (Wyeth) 0.2 mg. intramuscularly (Thompson's ergostetrine); (c) ergometrine (Burroughs and Wellcome) (Dudley & Moir's ergometrine) 0.125 mg. intravenously 50 cases and 50 cases 0.5 mg. intramuscularly; and (d) basergin (Stoll's ergobasine) 0.2 mg. intravenously. Again a daily note was made regarding the involution, morbidity and the subjective symptoms of the patients.

RESULTS

Involution.—The criteria of involutional progress are the extent of the recession of the uterus; the general consistency of its musculature and the character and amount of the lochia.

In the control group (Fig. 1) it can be seen that the uterus is always palpable above the symphysis at the tenth post-partum day and that its height averages 7 cm. above this level.

The group of cases that received ergonovine in the form of ergotrate (Lilly) showed the most rapid decrease in the size of the uterus as compared with the control cases as well as the cases receiving other medications. This increased rate of involution was most apparent during the last few days of the hospital stay.

The next most rapid decrease was seen in the patients receiving ergoklonin (Wyeth). Another factor must be considered here. The uterus in a patient after exhibition of ergotrate, intravenously, almost immediately became very firm and hard and remained so throughout the puerperium. This did not happen in any of the other groups of patients. For the treatment of post-partum hemorrhage due to atony of the uterus, from our experiences, ergotrate is to be recommended for its immediate results in causing the contraction of boggy uterus and keeping it in this condition.

With the other preparations it was often found necessary because of subinvolution or slow action to exhibit some other drug such as pituitrin or ergotrate either immediately or sometime during the hospital stay. The least desirable preparation from this point of view was ergometrine (Burroughs and Wellcome). Here, in 80 per cent of the cases it was necessary to use some other oxytocic. In the series of cases with basergin this was not as marked, although in 62 per cent of the cases it was found necessary to use ergotrate in order to prevent a subinvolved boggy uterus.

*We are indebted to Lilly & Co. for the supply of ergotrate; to John Wyeth & Bro. for the ergoklonin, to Burroughs and Wellcome for the ergometrine, and to Sandoz for the basergin.

SUMMARY

1. High blood pressure (140 systolic or above) as the first clinical sign of toxemias of late pregnancy is presented.
2. High and rising blood pressure as indicative of an increasing and possibly a fatal pregnancy toxemia is discussed.
3. A dosimetric schedule for the use of nembutal based on the height of the blood pressure as a suggestive method of treatment is submitted.
4. The results of 60 cases of late pregnancy toxemias effectively treated with nembutal by the above scheme without the occurrence of convulsions, apoplexy, or death are reported.

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619 FLORIDA AVENUE

CLINICAL EXPERIENCES WITH ERGONOVINE

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THE chemistry of ergot has been the subject of many recent investigations and various alkaloids and amines have been described which possess biologic activity. In 1932 Moir¹ of London clearly demonstrated the presence of a hitherto unrecognized substance in ergot which showed prompt oxytocic action when orally administered and was found to be distinct from ergotoxine and ergotamine. This was substantiated by Dale.² Working independently, Davis, Adair, Rogers, Kharasch and Legault³ of the University of Chicago isolated an active principle of ergot which they called "ergotocin."

Shortly after the appearance of this paper by Davis and his associates, Dudley and Moir⁴ reported the crystallization of their product which was named "ergometrine." At the same time working in Baltimore, Thompson⁵ isolated another principle which he called "ergostetrine." Finally Stoll and Burkhardt isolated "ergobasine." From the present available evidence it appears that ergotocin, ergostetrine, ergometrine, and ergobasine are the same. In fact all the investigators, each of whom independently discovered this new alkaloid of ergot, after investigation, acknowledged that the active principles each had isolated were identical.⁶ In view of this, the Council on Pharmacy and Chemistry of the American Medical Association in session March 14, 1936,⁷ decided it necessary to coin the new nonproprietary and not therapeutically suggestive name for this ergot alkaloid, "ergonovine." Meanwhile the various pharmaceutical houses had already capitalized the new findings: Lilly in the form of ergotrate; Wyeth in the form of ergoklonin; Burroughs and

Ergotrate is considered to be the drug of choice. In this group there was immediate contraction of the uterus, the lowest morbidity, the smallest number of patients complaining of pain and the most sustained firm contraction of the uterus.

CONCLUSION

Because of the degree of involution of the post-partum uterus; the control of bleeding; the resulting firmness of the uterus and the lessened morbidity, ergonovine in the form of ergonovine malleate (ergotrate, Lilly) one ampoule (0.2 mg.) should be given intravenously immediately after the birth of the placenta. In the post-partum hemorrhage, due to atony of the uterus, this should be given before packing is instituted. Often it will be found that packing is not necessary.

In cases of subinvolution ergotrate will be found of value.

We are indebted to Dr. Meyer Rosensohn for his stimulation, kindly interest, and helpful suggestions in the preparation of this paper. Drs. J. Weisberg, M. Miller, and J. Alkoff, erstwhile residents on the obstetric division, aided in compilation of the figures.

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215 EAST GUNHILL ROAD
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Bauer and Meller: Hemophilia in Women, Wien. klin. Wchnschr. 50: 495, 1937.

The authors answer in the negative the question whether the hereditary rule, now generally accepted, applies to all cases of hemophilia. They think that there are families in which the hemophilic factor becomes manifest only in males, that occasionally there are families in which the men and the women show hemophilic symptoms, and that in rare instances only the women exhibit the symptoms. The time is not yet ripe for the formulation of definite laws of the hereditary transmission of hemophilia. To be sure, severe and fatal hemorrhages as frequently occur in hemophilic men are only rarely observed in women. They describe four women whose disorder was characterized by a symptomatology similar to that of hemophilia as well as by a weakness of the thrombocytic apparatus. A combination of hemophilia and thrombopenia may occur and it is not justified to draw sharp distinctions between these two disorders. It may be assumed that the female sex organs provide a specific protection against fatal hemorrhages.

J. P. GREENHILL.

Ergoklonin while somewhat slower in action and therefore unsuitable for post-partum hemorrhage yet gave a fairly firm involuted uterus in about six to eight minutes after injection.

Bleeding.—A striking difference in the character of the lochia was noted on the discharge examination on the tenth post-partum day. The best results were obtained with ergotrate since 90 per cent of that group had no sanguineous discharge. In the control cases only 30 per cent were entirely free of bleeding. In the groups using ergometrine and basergin the percentage was the same as that in the control cases.

Morbidity.—A patient was considered morbid when her temperature reached 100.4° F. any two times after the first day post partum. These figures are corrected and constitute all temperatures of an obstetric nature that appeared in these 450 cases. The morbidity was highest (25 per cent) in the patients who received ergometrine and lowest (2 per cent) in the patients who received ergotrate; the ergoklonin series differed only slightly (4 per cent) from the ergotrate. In the patients receiving basergin the morbidity was 18 per cent.

Subjective Symptoms.—With ergoklonin, over 65 per cent of the women had pain, varying in intensity from mild to severe and limited to the first six days of the puerperium. In the ergotrate group this pain was experienced in only 12 per cent of the patients; while in the patients receiving ergometrine and basergin there was no pain. This would seem to imply perhaps a too tonically contracted uterus with the powerful ergotrate or ergoklonin.

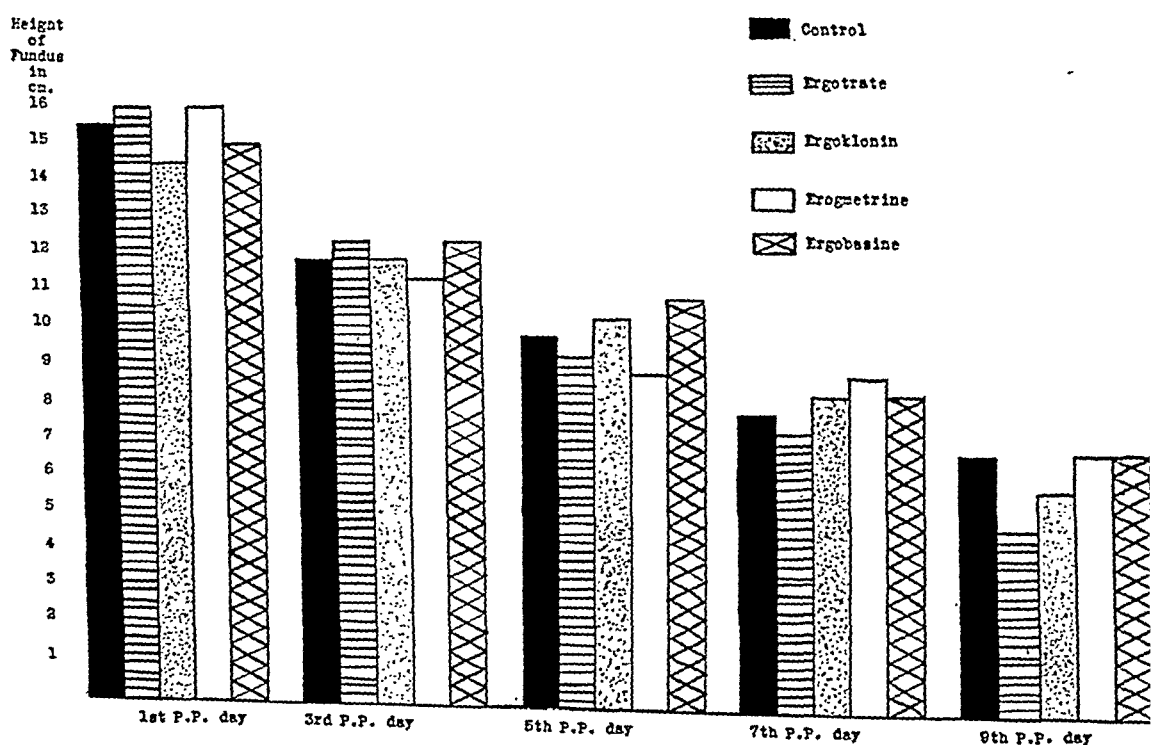


Fig. 1.—Height of fundus in centimeters above symphysis post partum, graphically shown after administration of various oxytocics.

DISCUSSION

The administration of ergoklonin gives all that can be desired in rapidity of involution, yet the annoying symptom of pain in 65 per cent of the women must be considered.

In this series ergometrine and basergin are shown to be of least value because of their unreliability in contracting the uterus. It is in these groups also that we find the greatest morbidity.

clot. The uterus was of normal size and the left tube and ovary appeared normal. The right tube and ovary were removed.

Pathologic Report: (No. 102100.) (Dr. James R. Cash.) Specimen consisted of the right tube and ovary, which formed a mass weighing 55 gm., adherent to which was a mass of beef red-appearing tissue, which seemed to be bulging from the lumen of the tube.



Fig. 1.—($\times 200$.) Section near fimbriated end of tube showing chorioepithelioma lining the lumen and invading the wall of the tube.

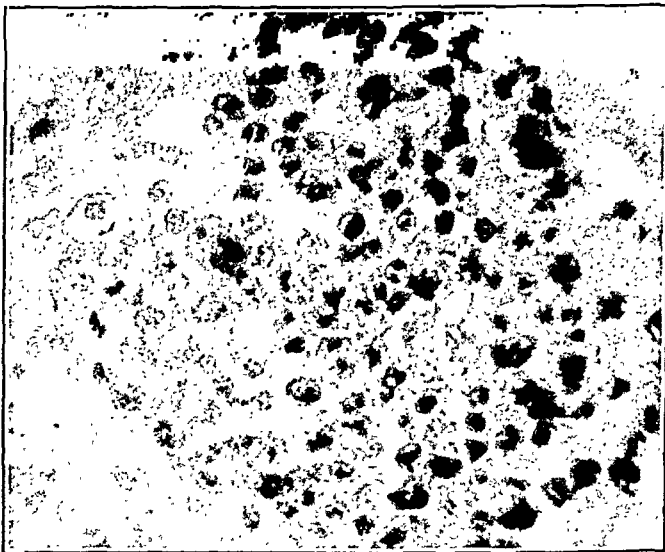


Fig. 2.—($\times 390$.) Higher power of tumor showing group of Langhans' cells surrounded by syncytium.

Microscopic Examination.—In the ovary there were numerous small Graafian follicle cysts, which contained pink-staining coagulated fluid. The stroma of the ovary was very fibrous and edematous, and lightly infiltrated with lymphocytes. There were numerous old scars of corpora albicantia, some of which showed pigmentation with iron. Closely bound to the ovary by dense granulation tissue was the Fallopian tube, the wall of which was considerably thickened and heavily in-

CHORIOEPITHELIOMA OF THE FALLOPIAN TUBE

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MARCHAND¹ in 1895 recorded the first instance of a chorioepithelioma of the Fallopian tube. Nurmberger² in 1932 stated that 33 authentic cases had been reported through 1930. He, however, did not include the case of Hartz³ which he considered questionable, and the case of Moore,⁴ both of which may be classified as tubal chorioepitheliomata. Since that time six additional cases have been reported by Stein,⁵ Fleurent and others,⁶ Savignoni,⁷ Grudzew and Russky,⁸ Bunnag and Bachman,⁹ and Bianchi and Arrillaga,¹⁰ making a total of 41 recorded cases. To this number we wish to add the following case:

CASE REPORT

Mrs. E. N. (No. 97777), aged twenty-three years, was admitted to the University of Virginia Hospital on June 14, 1932, complaining of a bloody vaginal discharge of six months' duration and a sharp pain in the right lower abdominal quadrant of three weeks' duration. The patient had been married for three years and had one child born in December, 1930, eighteen months previous to admission. The baby was nursed for three months and weaned in March, 1931. The menstrual periods recurred in June, 1931, three months after weaning, after which they recurred at regular monthly intervals with an average duration of seven days until December, 1931. The December period began at the usual time, but continued as a bloody vaginal spotting from that time until admission to the hospital in June, 1932.

The abdominal pain began first in February, 1932, in the right lower quadrant, at first quite acute and subsequently gradually subsiding. Three weeks before admission the pain recurred with sufficient severity to require confinement to bed, and was said to be associated with nausea, vomiting, chills, and fever. The appendix had been removed seven years previously.

At the time of admission the blood pressure was 115/65, temperature 98.8° F., hemoglobin 75 per cent Dare, red blood cells 4,585,000, white blood cells 4,036, and blood Wassermann negative. The examination revealed some generalized abdominal tenderness, although it was more marked in the right lower quadrant. An old scar of the appendectomy was present. The cervix was slightly patulous and showed small transverse lacerations. The body of the uterus was anterior, about normal size, somewhat limited in mobility with pelvic sensitiveness on attempts at movement. Nothing was palpated in the left adnexal region, while to the right of the uterus a soft, cystic, tender, fixed mass the size of an orange was outlined. There was moderately profuse uterine bleeding at the time of the vaginal examination.

The diagnosis seemed to hinge between an ovarian cyst, possibly intraligamentary, an old ectopic pregnancy, or a tuboovarian abscess.

June 18, 1932. *Operation:* Dilatation and curettage were done but no tissue was obtained. Exploration of the pelvis through an abdominal incision showed a mass the size of an orange in the right adnexal region, adherent to the omentum and intestines. After the separation of the adhesions the mass was found to be composed of the right tube and ovary, on the superior surface of which was an area about 5 by 7 cm., composed of dark brown degenerative tissue which suggested an old blood

December 12, 1932. Weight 100 pounds; felt well. The pelvis and vagina were free of masses and nodules. Friedmann's, negative.

May 22, 1933. A letter received from the patient stated that she was feeling well; weight 117 pounds.

Sept. 13, 1933. The patient had no symptoms. An x-ray of the chest was reported as suspicious of metastatic malignancy, but not pathognomonic. Friedmann's, positive. No masses or nodules were present in the pelvis or vagina. A neurologic examination and an examination of the eye grounds revealed normal findings. Sept. 19 to 22, 1933. X-ray therapy, 1890 r. given over pelvis, and 1,260 r. given over chest.

Jan. 1, 1934. Friedmann's, positive. An x-ray of the chest reported as suspicious for metastatic malignancy but not pathognomonic. X-rays of the skull and the pelvic bones were negative for metastases. The visual fields and eye grounds were normal. General physical examination was normal. The pelvis and vagina were free of masses and nodules. Jan. 5 to 14, 1932. X-ray therapy, 1,890 r. given to the pelvis and 2,500 r. to the chest through two anterior and two posterior portals.

March 15, 1934. Friedmann's, strongly positive. The pelvis was free except for some fullness rather high on the left side of the pelvis. X-ray of the chest showed findings which were consistent with metastatic malignancy. The eye grounds were clear. March 19 to 30, 1934. X-ray therapy, 5,000 r. units given over the chest through four portals. March 30, 1934. An x-ray of the chest showed the findings to be less marked and not as suggestive of metastatic malignancy as at the time of the previous examination two weeks ago.

April 9, 1934. A letter was received, which stated that the patient was paralyzed on the right side.

April 28, 1934. Patient died at home, apparently from brain metastases one year and ten months after the original operation and diagnosis. No postmortem examination was obtained.

NOTE: The patient lived about 250 miles from the Hospital and was practically indigent, and in the early days of her illness rather uncooperative, which accounts for the delay in completing the treatment in the early stages of the disease, and for the prolonged periods of absence during the follow-up procedures.

DISCUSSION

Extrauterine chorioepithelioma may originate either as a primary growth following an extrauterine pregnancy, or as a so-called ectopic chorioepithelioma, the villi having been transported during and subsequent to a previous uterine pregnancy, without initial malignant tumor formation in the uterus. It may of course be metastatic, from a primary malignant growth in the uterus, or teratogenous in which the tumor arises from chorionic cells included in a teratoma. To these generally accepted modes of origin of extrauterine chorioepithelioma, Hamdi¹¹ has recently suggested the possibility of its histogenesis from rudimentary rests, or by metaplasia.

The metastatic chorioepitheliomata secondary to a primary growth in the uterus are ordinarily not included in the discussions of primary chorioepithelioma of the Fallopian tube. Those of teratogenous origin most commonly arise in the ovary, teratomata usually forming the point of origin of chorioepitheliomata of the ovary and the subsequent metastatic lesions in individuals in whom no pregnancies have occurred. The majority of instances of tubal chorioepithelioma are of the primary type, arising in the tube subsequent to a tubal pregnancy. In support of this contention, Meyer¹² has pointed out the occurrence of hydatidiform degeneration of chorionic villi in instances of tubal gestation.

The ectopic type of chorioepithelioma of the tube, in which the villi have been transported, subsequent to a previous intrauterine pregnancy, without a primary tu-

filtrated by lymphocytes, mononuclears, and an occasional plasma cell. Arising from the wall of the tube was a large mass of partially calcified, very old granulation tissue, heavily infiltrated with lymphocytes filled with hemosiderin. Also arising from the distorted wall of the tube was a rapidly growing tumor composed of branching anastomosing cords of syncytium, partially surrounding small nests of more deeply staining Langhans' cells. These cells invaded the wall of the tube extensively, masses of tumor cells being intermingled with masses of degenerating smooth muscle and remains of rugae. A large portion of the tube was necrotic and very hemorrhagic.

Diagnosis: Chorioepithelioma of Fallopian tube. The immediate postoperative convalescence was uneventful. June 24, 1932: Friedmann's test, positive. June 30, 1932: Friedmann's test, positive. An x-ray of the chest was reported as negative for metastatic malignancy. Total hysterectomy with left salpingo-oophorectomy and radiation therapy over the pelvis was advised, but the patient refused any further procedures at the time and left the hospital, but promised to return.

July 22, 1932. The patient was readmitted to the hospital. She had been feeling well since leaving the hospital, and there had been no recurrence of the pain or bleeding. Vaginal examination showed the body of the uterus anterior, perhaps slightly enlarged, and pulled toward the right side. There was a definite induration to the right and posterior to the uterus. Nothing abnormal was felt in the left adnexa. Friedmann's, strongly positive. An x-ray of the chest was reported as negative for metastatic malignancy.

July 26, 1932. Operation: Exploration of the pelvis showed the uterus small and movable. The left ovary contained a cyst the size of a lemon. The ileum was adherent to the right broad ligament where adhesions had been separated at the time of the previous operation. Total hysterectomy and left salpingo-oophorectomy were done.

The postoperative convalescence was complicated by separation of the abdominal incision and extrusion of the intestines on the ninth postoperative day. Secondary closure was done and was followed by an uneventful convalescence.

Pathologic Report (Dr. James R. Cash): Specimen consisted of uterus, left tube, and left ovary, with a combined weight of 110 gm. The uterus and endometrium appeared grossly normal. The ovary contained a hemorrhagic cyst 6 by 4½ by 5 cm., which on section appeared multilocular and contained a yellowish thin serous fluid. The tube appeared normal.

On microscopic examination the sections of the uterus and tube appeared normal. The endometrium seemed premenstrual in character. The wall of the cyst of the ovary was composed of fibrous ovarian stroma, and was lined by layers of large polyhedral cells resembling lutein cells.

Diagnosis: Normal uterus and tube, lutein cell cyst of ovary.

August 17, 1932. Friedmann's, strongly positive.

The patient refused x-ray therapy on this admission and left the hospital on Aug. 17, 1932.

October 21, 1932. The patient reentered the hospital. Since the previous admission she had been feeling well, had no complaints, and was gaining weight. Vaginal examination revealed the vagina and pelvis to be free of any nodules or masses. An x-ray of the chest was negative for metastatic malignancy. Friedmann's, strongly positive. October 25 to 29, 1932. X-ray therapy (200 K. V., ½ mm. copper and 1 mm. aluminum), 1,890 r. units given to the pelvis through three portals and 270 r. units given over posterior chest. She was discharged from the hospital on Nov. 1, 1932.

chorioepithelioma of the Fallopian tube may be considered as a fatal disease, as there may be considerable question concerning the permanence of the recovery in the recorded cases. As exemplified by our patient, the mere survival without symptoms for a year or so does not necessarily mean recovery.

SUMMARY

An instance of chorioepithelioma of the Fallopian tube, which was treated by operation and radiation, is reported. This seems to be the forty-second case to be recorded in the literature.

The modes of origin of extrauterine chorioepitheliomata are discussed, and it is believed that in our patient it developed primarily in the tube subsequent to a tubal pregnancy.

The value of tests for the luteinizing hormone in the urine in cases of chorionic tumors is shown. A persistent positive reaction even in the absence of all signs and symptoms seems to indicate a serious prognosis, while too much reliance should not be placed in a single negative test.

The mortality in the reported cases has been about 93 per cent.

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THE MANAGEMENT OF PREGNANCY AND LABOR COMPLICATED BY TRIPLETS*

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(From the Preston Retreat)

THIS record of a triplet pregnancy is presented not as a "case report," but as instructive experience derived from unusual behavior, study, and management of a potentially dangerous condition. A review of the fate of triplets (all unreported) in three institutions attended by the author discloses interesting facts. In the Philadelphia Lying-in Hospital from 16,857 births of over twenty weeks' gestation two sets of triplets have occurred.

The first patient, para ii, delivered at thirty-one weeks: A, male, O. R. A., 4 pounds 1½ ounces; B, male, occ. post., 1 pound 12 ounces; C, female, footling, 3 pounds 10 ounces; pregnancy was featured by weight increase in the last four months from 126¼ to 162 pounds, and by maximum blood pressure of 156/94; labor was

*Read at a regular meeting of the Philadelphia Obstetrical Society, May 6, 1937.

mor in the uterus, is unusual. Fleurent, Keller and Meyer⁶ have pointed out that there are no instances of ectopic tubal chorioepitheliomata with certainty. Naturally in tubal chorioepithelioma it is often quite difficult to disprove the occurrence of an early tubal pregnancy, which might have been the origin. While it is impossible to prove that chorioepithelioma of the tube or ovary is of the ectopic type, on the other hand the possibility of its occurrence is shown by instances of chorioepithelioma of the broad ligament without demonstrable evidence of chorioepithelioma elsewhere, unless one assumes that the original uterine growth had spontaneously disappeared. One such patient was under our care, in whom several months after an abortion, a pelvic mass was found. A curettage of the uterus was done and no tissue was obtained which suggested chorionic cells. Examination of the uterus, tubes, and ovaries through an abdominal incision revealed entirely normal structures to inspection and palpation. The mass in the pelvis was an inoperable hemorrhagic tumor of the right broad ligament. While at that time the diagnosis was not confirmed either by biopsy or the Aschheim-Zondek test, the patient developed pulmonary metastases and died about two months after the exploratory operation, in spite of radiation therapy. Unfortunately no postmortem examination was done, and it is possible that a small focus of malignant chorionic cells existed in the uterus, although on curettage and on gross examination of the pelvic structures there was no evidence of tumor growth or nodules. Assuming that the diagnosis of chorioepithelioma was justified, and with the absence of any demonstrable tumor in the uterus, this would have to be considered as an instance of ectopic chorioepithelioma due to the transportation of villi during and subsequent to the abortion some months previously.

In our present case the tumor may have been primary, following an early tubal gestation or ectopic from transported villi during and subsequent to the pregnancy eighteen months previous to the first admission to the hospital. It most likely followed an early tubal pregnancy which probably occurred in December at the time the vaginal bleeding began, and which was very likely partially aborted from the tube in February at the time of the severe abdominal pain, which gradually subsided. The recurrence of the severe pain three months later (three weeks before admission to the hospital) was associated with the growth, invasion, and extrusion of the malignant chorionic cells at the fimbriated extremity of the tube.

The life cycle of a tubal chorioepithelioma is usually considered as divisible into three periods: first, that of the extrauterine pregnancy, second, a latent period, and third, the period of tumor growth. Assuming our case was one following an extrauterine pregnancy, it may be easily divided into these three periods, the period of extrauterine pregnancy from December, 1931, to February, 1932, the latent period from February to May, and the period of tumor growth from May onward.

The findings on the Friedmann test are of interest in our patient, as after numerous positive tests it became temporarily negative, following the complete operation and pelvic and abdominal radiation. It was found positive again nine months later and remained positive until death in spite of extensive radiation therapy. The pregnancy urine test is of great value in the diagnosis and prognosis of chorionic tumors. For a period of several months the only evidence that a cure had not been effected in our patient was the presence of a positive Friedmann's test. The single negative finding stimulated an optimistic outlook for her future, which proved to be false and led to a sense of security which was not justified.

Of the cases reported in the literature possibly three patients may have recovered from the disease. The patient of Albert¹³ was well one year at the time of the report. Lofquist's¹⁴ case is recorded as a recovery and Miles Phillips'¹⁵ patient had survived for something over two years. Assuming that these instances may be considered as recoveries, it gives a mortality of about 93 per cent. In general, however,

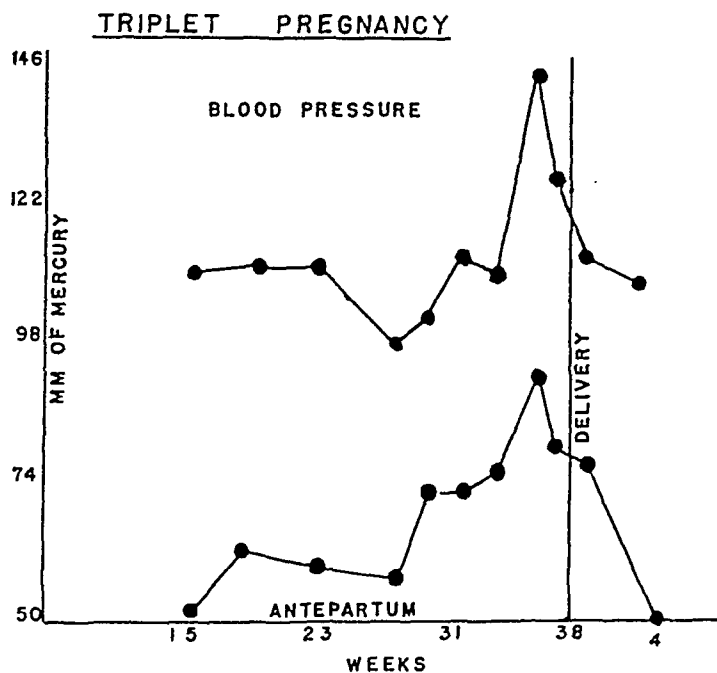


Fig. 1.—Moderate hypertension at thirty-sixth week.

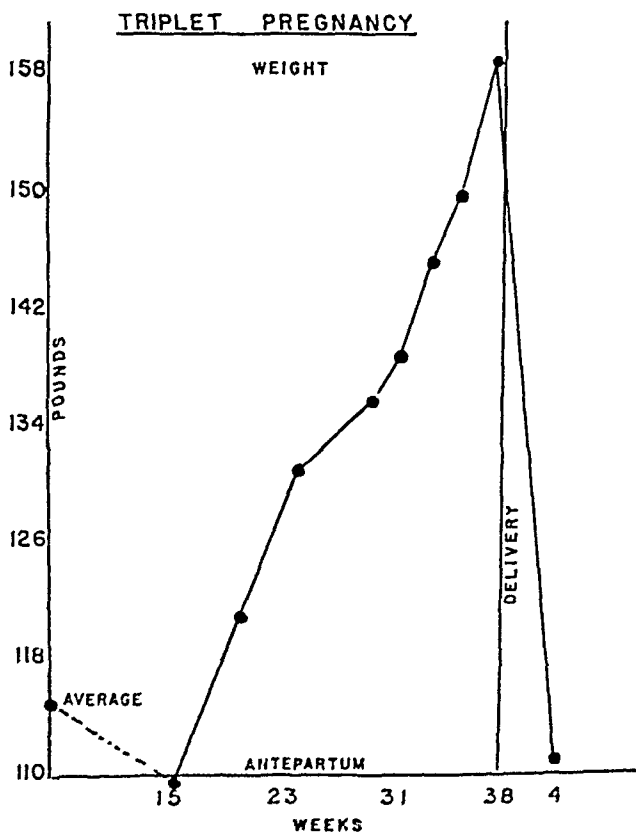


Fig. 2.—Rapid weight increase with general edema in spite of fluid balance efforts.

rapid, first and second stages only three hours thirty-seven minutes, third stage fifty-seven minutes; delivery was simple; puerperium uncomplicated; infants all survived (Dr. Robert A. Kimbrough). The second patient, para iii, delivered "under thirty weeks": A, male, O. L. A., 2 pounds 12 ounces; B, male, O. L. A., 2 pounds 14 ounces; C, male, "version," 2 pounds 8 ounces; pregnancy uneventful, patient recalcitrant; labor slow, first stage nine hours, second stage two hours fifty-five minutes, third stage uncomplicated; delivery satisfactory; recovery normal; infants all died from prematurity.

In the Hospital of the University of Pennsylvania the last 15,000 viable deliveries produced 1 set of triplets from a para i, aged twenty-six, who was delivered at thirty-one weeks of one female and two male infants, the first by outlet forceps; pregnancy normal; labor vague, "several days," delivered 7.75 hours after rupture of membranes "without contractions," forty-five minutes between infants, third stage ten minutes; puerperium complicated by prolonged morbidity (endometritis); infants, 1 stillborn, 1 died on the fifth day, and the third unknown.

In the Preston Retreat, among 16,500 pregnancy registrations beyond twelve weeks of gestation there has appeared but one set of triplets. The record of this case is briefly summarized below to illustrate the following features: (1) New prenatal plan in supporting multiple pregnancy; (2) prolongation of triplet pregnancy to the thirty-eighth week of gestation; (3) marked bilateral hydronephrosis due to large pregnancy, resulting in: (4) distorted phenolsulphonephthalein and indigo-carmin urinary functional tests; (5) no proportional increase in quantitative estrogenic substance and anterior pituitary-like urinary hormone analysis; (6) abruptio placentae between births of second and third infants; (7) unusually fine and large triplets.

Oct. 3, 1936: Mrs. M. K., aged twenty, married to a slight man of twenty-one years, stated that no multiple pregnancy had occurred in either immediate family. The mother had carried and spontaneously delivered one living child without any complication, registering with this second pregnancy in good condition on the above date; due for confinement March 21, 1937.

General physical examination disclosed a well-developed young woman, height 5 feet 3 inches, with normal heart and lungs. The obstetric examination was also favorable, the only features as of October 3 being slight edema of the right leg, moderately relaxed birth canal, and average gynecoid pelvis.

Until February 1, the prenatal progress was subjectively and objectively good, although cervical cauterization, treatment for secondary anemia (hemoglobin 65 per cent—Dare), dental attention and anodyne for left abdominal parietal neuralgia were administered. On February 1, at thirty-third week of gestation, the patient was admitted to the hospital ward on account of excess weight gain (see), and severe persistent bilateral ankle edema, for fluid control, rest, restricted salt ingestion, mild catharsis, urea diuresis, and high mineral-vitamin diet including extra beef, milk, eggs, dicalcium-phosphate with viosterol, and capsules of vitamins A, B, D, and G. The urine remained virtually negative, showing only a faint trace of albumin in one out of twelve examinations, and no other abnormality, although the sp. gr. averaged

The placenta proved to be monochorionic or uniovular, weighed 1,364 gm. and measured 22 by 24 by 4 cm. The infants were identical females, all amazingly healthy and vigorous, weighing 2,286, 2,409, and 2,427 gm., respectively. Last heard from, they were thriving perfectly at six months of age, continuing on acidified evaporated milk, dextrimaltose, and soluble irradiated ergosterol.

The puerperium was abnormal chiefly from severe secondary anemia requiring two transfusions, plus slight sapremic morbidity associated with lochiometra. Twenty-seven days after delivery a second cystoscopic investigation was completed, which showed no bladder or ureteral orifice pathology, and only slight hydronephrosis of the right ureter, a striking contrast to the prior examination two days before birth, when there was great edema and congestion of the trigone, very high and divergent ureteral orifices and bilateral extreme nonobstructive hydronephrosis (see Table II). The mother's condition on discharge was excellent. There was only 2 fingers' diastasis of the recti abdominis muscles and no renal ptosis. The lochia had ceased, the uterus had involuted in good position to 3 fingers above the symphysis pubis, while the remainder of the birth tract was exactly as before.

TABLE I. ABDOMINAL MEASUREMENT BEFORE AND AFTER DELIVERY

HEIGHT—61 $\frac{1}{4}$ IN. OR 155.6 CM.		
	37TH WEEK A.P.	5TH WEEK P.P.
Circumference at umbilicus	42 in.—106.7 cm.	29 in.—73.7 cm.
Symphysis to ensiform	22 in.—55.9 cm.	9 in.—22.9 cm.

TABLE II. CYSTOSCOPY

		37TH WEEK A.P.	5TH WEEK P.P.
Retention	Right	79 c.c.	11 c.c.
	Left	96 c.c.	None
Injection	Right	Not done	31 c.c. (Recovered)
	Left	Not done	7 c.c. (Recovered)
Function (Indigo-carmin)	Right	23 Min.-(Light)	7 Min. (Dark)
	Left	19 Min.-(Light)	7 $\frac{1}{4}$ Min. (Dark)
Microscopy	Right	Occ. W.B.C.; 3-5 R.B.C. many bac.; many gram (-) rods.	Few pus cells. Mod. squamous. Mod. gram + cocci No T.B.
	Left	Occ. R.B.C. and mucus; many bac. Many gram (-) rods; occ. gram + cocci (Hem. staph.)	Not done

TABLE III. TWENTY-FOUR-HOUR URINARY HORMONE ASSAY. QUANTITATIVE VALUES AT THIRTY-SIXTH WEEK MODERATELY INCREASED, BUT NOT IN PROPORTION TO PLACENTAL MASS

<i>Estrin</i> : Active, 2,000 Rat units
Combined, 4,000 Rat units (Active plus inactive)
<i>Prolan B</i> : 3,200 Rat units

only 1.014. Directly after admission, a positive twin, possible triplet diagnosis was made; the latter was confirmed by x-ray film, yet never were more than two fetal heart sounds audible, the greatest variation being 9 beats per minute.

On March 4, one amniotic sac ruptured spontaneously at 4:00 A.M., and labor began fifteen minutes later, progressing very actively to second stage at 7:15 A.M. The infants were delivered at 8:12 A.M., 8:23 A.M., and 8:31 A.M., each, after arti-

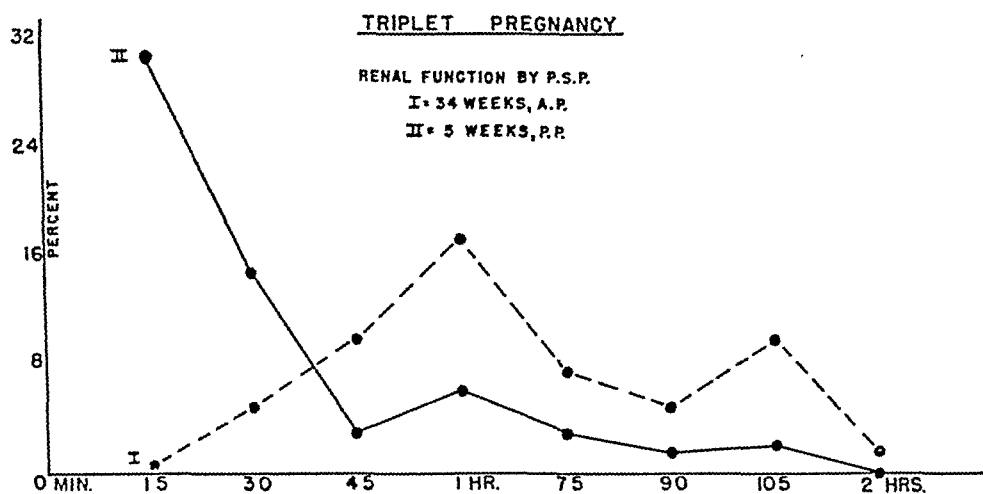


Fig. 3.—Ascending “hydronephrotic” antepartum, and normal steep descending postpartum curve after intravenous phenolsulphonethalein injection.

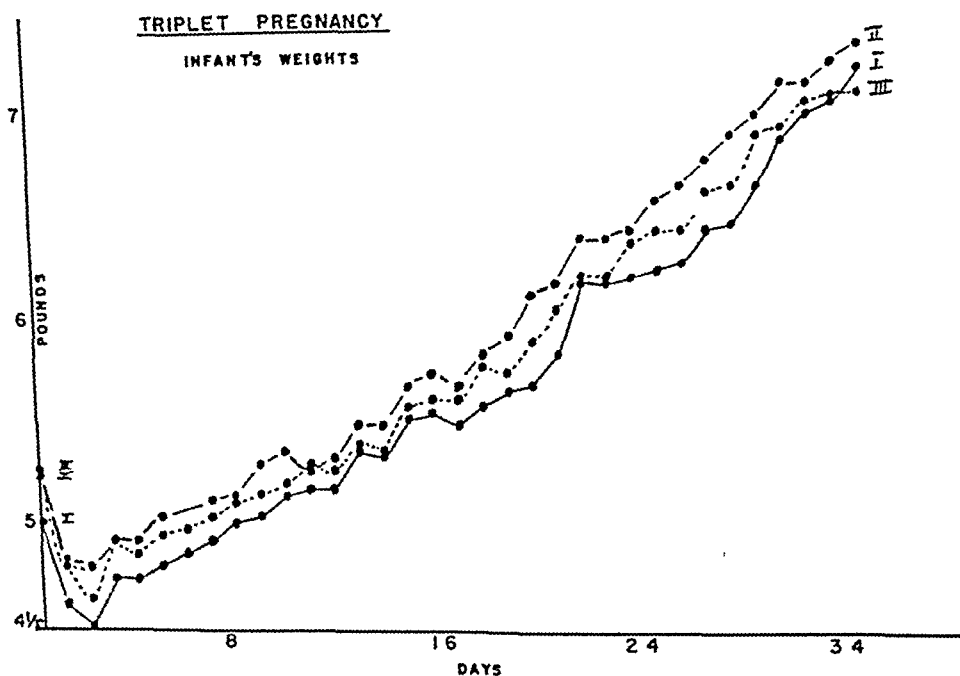


Fig. 4.—Amazingly vigorous identical female infants. Placenta, monochorionic (monozygotic).

ficial rupture of the second and third amniotic sacs, by easy manual rotation from O. R. P., O. R. P., and O. L. P., followed by low Tucker-McLane forceps extraction without injury. However, sharp bleeding with the birth of the third infant, followed by immediate descent of the placenta to the introitus and simple expression in Schultze mechanism indicated complete abruptio placentae during the last delivery.

present in the ovary. The ovariectomized animal injected with ovarian follicular hormone shows that the growth characterizing the rest of the genital tract in response to this stimulation also extends up into the tubes. Growth is especially active in the fimbriated ends. It is difficult even with the colchicine method to find many mitoses in the uterine end of the tube. The illustrations show the high incidence of mitotic figures in the uterine tubes of the monkey. At least twelve mitotic

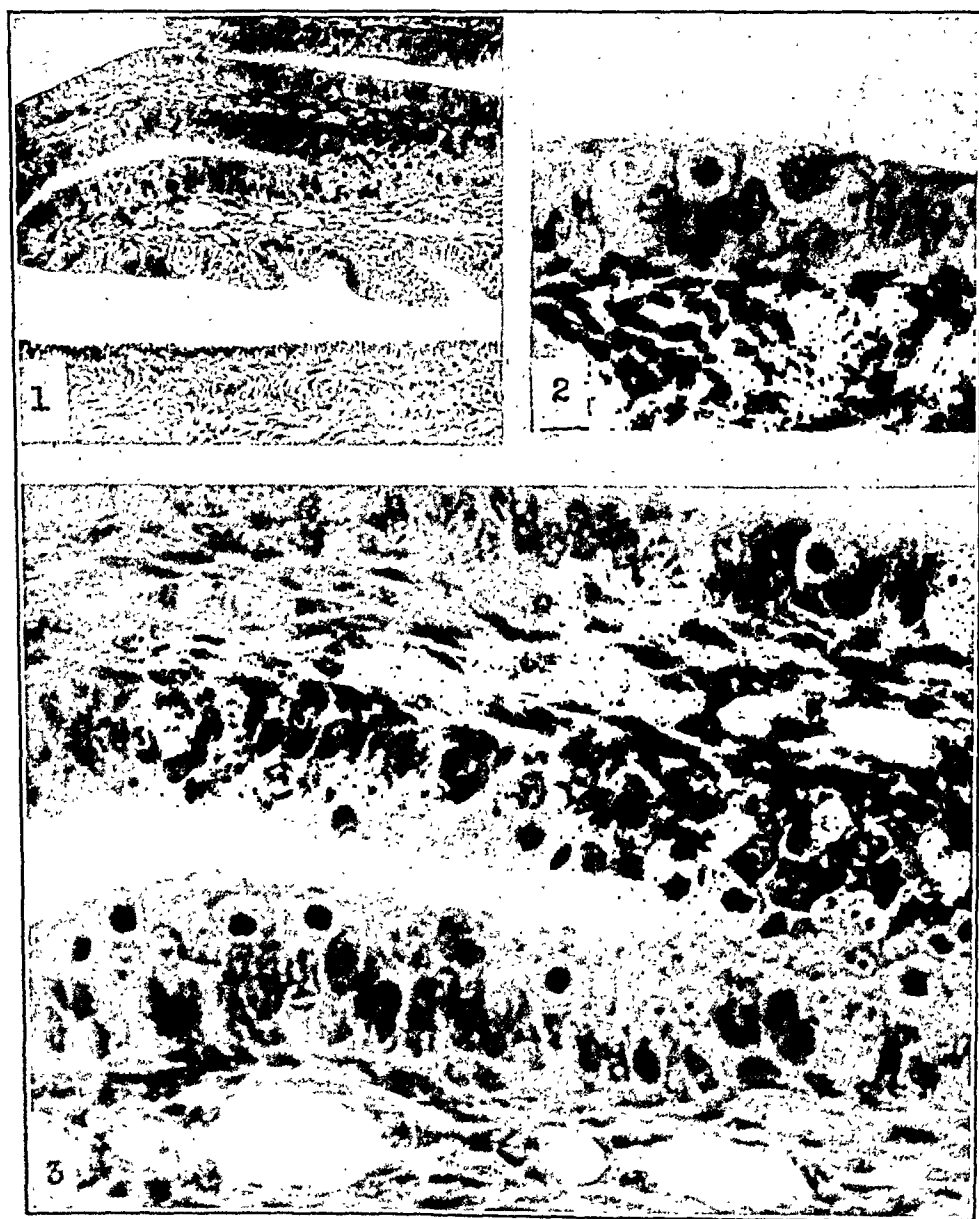


Fig. 1.—A portion of the fimbria of a uterine tube of a monkey. Many mitotic figures are found in the epithelium, being particularly numerous in localized areas. The germinal epithelium of the ovary seen in the lower part of the photomicrograph shows no mitotic activity.

Fig. 2.—A photomicrograph of a small portion of the tubal epithelium showing a polar view of a metaphase stage. Individual chromosomes may be recognized. The chromatin of a second dividing cell is clumped, as frequently occurs in cells influenced by colchicine.

Fig. 3.—Higher magnification of Fig. 1, above.

CONCLUSIONS

1. It is possible to carry triplet pregnancy close to maturity and to secure vigorous infants.

2. Hospital study and control from at least thirty-four weeks' gestation is necessary, including rest, high protein-mineral-vitamin, and low salt-water diet.

3. Hydronephrosis of multiple pregnancy in the last trimester precludes accurate urinary excretion renal function tests, and possibly interferes with quantitative twenty-four-hour urinary hormone valuation. Further analyses of hormone content in urine and placental substance from multiple pregnancies will be helpful in determining their source values.

4. Premature separation of a normally situated and conditioned placenta must be considered in late triplet pregnancies.

HYPERPLASIA IN THE EPITHELIUM OF THE UTERINE TUBES

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I HAVE frequently sought for mitotic figures in the epithelium of the uterine tubes, after having been greatly impressed by the rapid growth of the vagina and uterus in response to the ovarian follicular hormone. Periods of retrogression occur paralleling the menstrual period in primates (Snyder, 1924; Allen, 1928) and the diestrus period in lower mammals (Allen, 1922; Snyder, 1923). These degenerative phases alternate with periods of repair and regeneration. Nevertheless, search for mitoses in the tubal epithelium has been very disappointing even though the vagina and uterus of the same animal may be growing rapidly.

With the use of the drug colchicine for the study of hyperplasia, it has been possible to hold dividing cells in metaphase, thus accumulating all cells dividing in a period of from ten to twenty hours (Allen, Smith and Gardner, 1936-1937). In this condition they are easily recognizable, making the count of mitoses for a mitotic index extremely convincing. While previously 10 to 20 mitotic figures per section might be considered an index of hyperplasia, with the colchicine method several hundred or even over a thousand may occur in a single cross-section of the vaginal epithelium of the mouse.

This new method has emphasized the epithelial hyperplasia in the uterine tubes of the mouse, rat, and monkey. Cell divisions are most numerous in the tubes of the normal animal when large follicles are

There were 220 white patients and 225 colored patients in this series of cases. The patients varied in age from seventeen years to forty-seven years.

In this group there occurred 51 deaths, 21 white patients and 30 colored patients, a mortality rate of 11.4 per cent. All age groups were affected proportionally to the age groupings of the entire series. The majority of the white cases occurred between the ages of 27 and 36 years, and the colored cases between the ages of 22 and 31 years in the entire series.

The greatest number of white patients were between the ages of 27 and 31 years while the colored patients were between the ages of 22 and 26 years, there being a five-year difference in the age groups. The white patients increase in number from 21 to 31 years, the colored patients start high at 22 and decrease in number to 32 years, just a reverse in the age groupings.

PREVIOUS INTRAUTERINE PREGNANCIES

There were 69 patients in this series who were nulliparous (15.5 per cent); 84 patients who had had one pregnancy (18.87 per cent); and so on, two patients having had 16 pregnancies.

The majority of the patients reported had never had a miscarriage (207 cases, or 46.51 per cent); 94 patients (21.12 per cent) had had one miscarriage; and on up to one patient, as seen reported, having had 10 previous miscarriages or abortions.

MENSTRUAL DISTURBANCES

The menstrual disturbances were quite variable. There were 78 patients (17.52 per cent) who gave a history of no irregularity of menstruation; 142 patients (31.91 per cent) who gave a history of one missed period; and 97 (21.8 per cent), two missed periods; and so on up to two patients who stated that they had not menstruated for eight months.

There were 45 patients (10.11 per cent) who gave a history of menorrhagia, and 30 patients (6.9 per cent) who gave a history of metrorrhagia.

TUBAL INVOLVEMENT

It is interesting to note how much more frequently the right tube is involved than the left in both the colored and the white races. This may be due to the frequency of appendicitis associated with perisalpingitis interfering with the normal physiologic peristaltic action of the tubal musculature. There is a slight torsion of the uterus to the right normally which may in some way also interfere with the peristaltic movements of the tube, thereby retarding progress of the impregnated ovum.

DURATION OF HOSPITALIZATION

The stay in the hospital in weeks was recorded, and it was found that the majority of the patients stayed over two weeks, the average stay being 18.6 days. There were, however, 36.4 per cent who left the hospital between seven and fourteen days. Almost all of the 8.26 per cent of patients recorded as staying less than a week died.

SYMPTOMS

The symptoms as presented by the patients on admission were varied, but those most frequently found were cramps or pains in the lower abdomen, bleeding, faint-

figures have been found in a single section of the fimbria adjacent to the germinal epithelium of the ovary (Fig. 1). Fig. 2 is a polar view of a metaphase stage showing the ends of individual chromosomes protruding from the mass, while at the left is a mitotic figure in which the chromosomes have been clumped, as frequently happens in cells influenced by this drug. Fig. 3 shows 10 mitotic figures in a restricted field. Polar and equatorial views can be noted and also several cells with the clumped chromatin.

SUMMARY

Waves of growth, especially evident in the epithelium, extend into the uterine tubes. They occur in normal animals when large follicles are present in the ovaries and are induced in ovariectomized animals by the follicular hormone. This is similar to, and coincident with, the hyperplasia in the vagina and uterus.

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TUBAL PREGNANCY

AN ANALYSIS OF 445 CASES

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THE tubal pregnancies which have occurred in the Charity Hospital in New Orleans have been reviewed several times in the past (*Am. J. OBST. & GYNEC.*, July and August, 1922). It is the purpose of this paper to bring the statistics up from the review of 1906 to 1920, by one of us, through 1936. In the files of the Charity Hospital Record Room there are 490 cases of ectopic pregnancy between the years 1919 and 1936. For this period, the total number of gynecologic admissions was 62,853, an incidence of 0.78 per cent of ectopic pregnancy. In this group of cases, 63 deaths occurred, a mortality rate of 12.8 per cent.

For the purpose of study only 445 records were available and this study is predicated on these records only. Of these 445, the earlier records are not as definite and complete as the more recent ones, and this explains some of the incomplete graphs and tables presented.

The transfusions given in the entire series are appended:

	CASES
None	287
One	86
Two	23
Three	6
Four	1
?	9
Autotransfusions	7

We feel hesitant about reporting the small number of transfusions which were given when we realize what a valuable therapeutic measure it is in this type of case. However, it must be appreciated that we are dealing with negro patients and with patients from all over the state of Louisiana, whose relatives are often difficult to contact for donors and when contacted are reluctant to give their blood. In the 51 patients that died, 9 transfusions were given preoperatively, and of these only 1 patient died before operation. The transfusions, however, were given immediately before operation or while the patient was on the operating table.

The sedimentation rate is known to be of definite and valuable aid in making a diagnosis of inflammation in the pelvis. On the few patients (12) who had a sedimentation rate recorded we found that in ectopic pregnancy it is not rapid as in acute infections, but remains prolonged, in our series averaging about forty-seven minutes.

This point bears out the contention of Dr. Paul Titus of Pittsburgh who makes the statement that in those patients with elevation of temperature and pulse rate with leucocytosis, the blood sedimentation test is of immeasurable value in helping one to make a differential diagnosis between ectopic pregnancy and acute inflammatory processes. It remains persistently prolonged within normal range.

ANESTHETIC

The anesthetics used on these patients were:

	CASES
Ethylene	100
Ether	214
Spinal	104
Local	5
Nitrous oxide	3
Epidural	4
None	1

Contrary to the general belief, ectopic pregnancy cases do as well under one form of anesthesia as another.

DEATHS

As stated before, there were 51 deaths in this series of cases. Twelve patients died before operation, 5 died on the operating table, and 34 died after operation.

Of the patients who died, 35.3 per cent were admitted in shock, 25.4 per cent in poor condition, 17.7 per cent in fair condition, and 21.4 per cent in good condition. The preoperative condition of the patients was analyzed: 24.8 per cent were operated upon in shock, 34.7 per cent in poor condition, 12.4 per cent in good condition, and 8.1 per cent in fair condition.

The preoperative medication in the patients who died was palliative in most instances, 27 cases (55 per cent); there were 10 patients (20 per cent) who received subcutaneous clyses; 5 patients (10 per cent) received intravenous infusion; 2 patients (4 per cent) received acacia with transfusions or infusions; and 7 patients (14 per cent) received blood transfusions.

The temperature of the patients who died was analyzed, and it can be seen that it ranged from 98 to 101° in the majority of cases, only a few patients showing a temperature as high as 104.

The lymphocyte count as recorded in some of the charts of the deaths ranged from 8,000 to 25,000 white blood cells.

ing, weakness, nausea, and vomiting. A list of the presenting symptoms is appended with the number of patients recorded as having had them:

<i>Pain:</i>	CASES	<i>Vasomotor Disturbances:</i>	CASES
Cramps in lower abdomen	123	Fainting	39
Acute pain in abdomen	113	Faintness	34
Pain in right side	50	Weakness	34
Pain in left side	37	Shock	9
Pain in lower left quadrant	34	<i>Disorders of G. I. Tract:</i>	
Pain in lower right quadrant	39	Diarrhea	9
Pain in back	15	Nausea	30
Pain	10	Vomiting	60
Pain about umbilicus	4	Constipation	3
Pain in upper abdomen	3	Lump in abdomen	18
Pain in shoulder	5	Swelling in abdomen	7
Labor pains	8	Tenesmus	11
Headaches	3	Dysuria	9
<i>Menstrual Disorders:</i>		Polyuria	1
Bleeding	149	Fever	4
Uterine cramps	4	Chills	2
Dysmenorrhea	2		

DIAGNOSIS

The diagnoses on admission were as varied as the symptoms presented would suggest, but in spite of these variable symptoms, 276 cases were diagnosed as ectopic pregnancy (62.02 per cent). Of the patients who died, the admission diagnoses were similar to those of the entire series except that there was less accuracy, only 51 per cent being diagnosed correctly.

A list of the admitting diagnoses is presented not to shame those of us who made them but so that others may see where confusion might arise and better their own statistics:

	CASES		CASES
Ectopic pregnancy	276	Dermoid cyst	1
Abortion	21	Left ovarian cyst	3
Chronic pelvic cellulitis	15	Acute indigestion	2
Bilateral salpingitis	11	Endometritis	2
Acute pelvic cellulitis	13	Cholelithiasis	1
Cystic ovary	16	Right salpingitis	1
Fibroids	22	Peritonitis	1
Pelvic abscess	6	Typhoid fever	1
Salpingo-oophoritis	12	Intestinal obstruction	1
Tuboovarian abscess	16	Ruptured uterus	1
Acute appendicitis	11	Prolapsed uterus	1
Chronic salpingitis	9	Puerperal sepsis	1
Pyosalpinx	5	Retroverted uterus	1
Subacute appendicitis	4		

The operations performed on these patients are listed:

	CASES		CASES
Right salpingectomy	147	Bilateral salpingo-oophorectomy and	
Left salpingectomy	78	fundusectomy	1
Right salpingo-oophorectomy	94	Right oophorectomy, dilatation and	
Bilateral salpingectomy and right		curettage, trachelorrhaphy;	
oophorectomy	8	perineorrhaphy	1
Bilateral salpingectomy	8	Salpingo-oophorectomy, Norris sus-	
Bilateral salpingo-oophorectomy	11	pension, appendectomy	1
Bilateral salpingectomy and left		Salpingo-oophorectomy, appendec-	
oophorectomy	5	tomy	2
Hysterectomy	8	Salpingo-oophorectomy, conization	
		of cervix, removal of condyloma	1

Of the 8 hysterectomies done, 5 of the patients died, indicating definitely that major surgical procedures should not be done in the presence of ectopic pregnancy.

On opening the abdomen the great omentum was found adherent to the anterior abdominal wall over the pubis. Loops of small intestine were matted together by fibrin. On the right side of the abdomen the enormously distended and paper thin colon appeared to *descend* into the pelvis, blocking approach downward. Behind it were numerous loops of ileum which likewise entered into the pelvis. Some of these loops were readily drawn upward, several coming out of the extra-abdominal hernial pouch which formed part of the prolapse and extended more than halfway to the patient's knees.

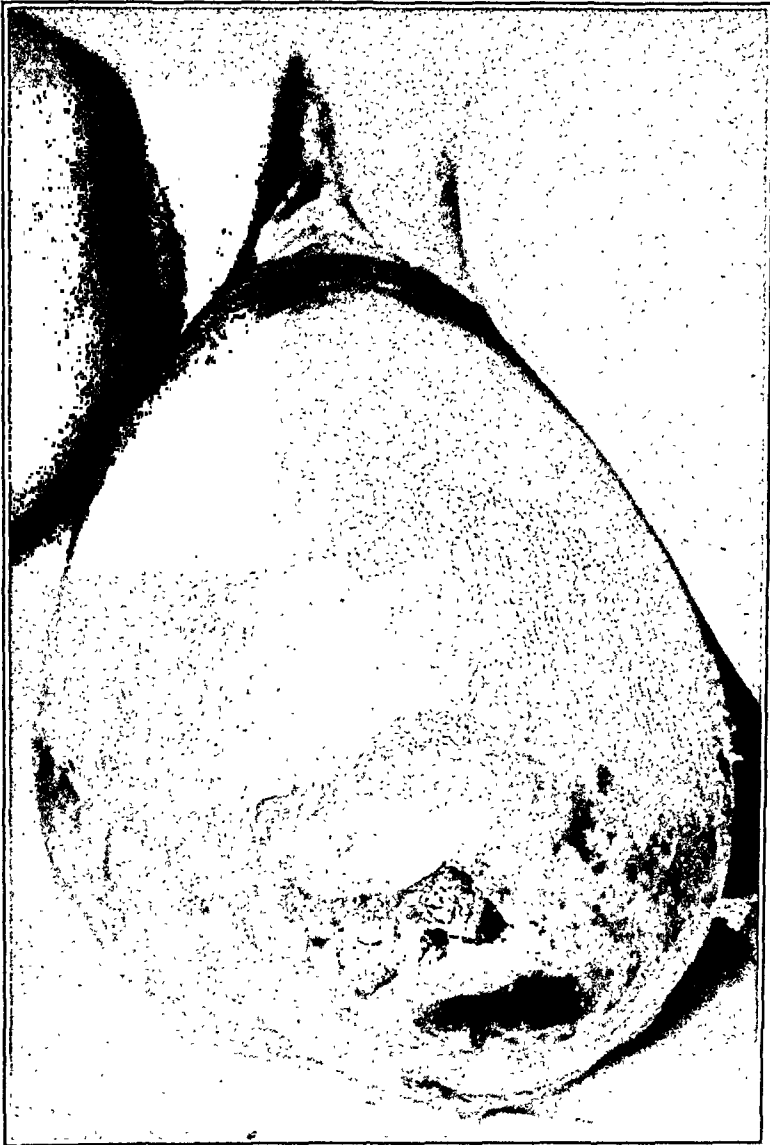


Fig. 1.—Prolapse with complete eversion of vagina.

In order to gain access to the pelvis and prolapse, after careful packing with moist compresses, a purse-string suture was placed on the distended bowel and through the center of this a large needle was inserted. Much gas was thus evacuated, and in the course of a few minutes the bowel collapsed. The needle was removed and the suture tied.

Now all accessible intestinal loops were freed and removed from the depths. The wall of one loop required repair. At the bottom of the sac which could only be reached by working the forearm downward, up to the elbow, an adherent transverse loop of collapsed ileum could be felt. Further exploration showed that the

IRREDUCIBLE, STRANGULATED, COMPLETE PROLAPSE OF THE UTERUS, COMPLICATED BY SLIDING HERNIA OF THE CECUM AND INTESTINAL OBSTRUCTION

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ALTHOUGH complete prolapse of the uterus, often complicated by enterocele, is of frequent occurrence, loss of reducibility and consequent incarceration is most infrequent.

A search of the literature, including a study of the older textbooks published before the operative era, shows but one report of conditions such as were encountered in this patient.

v. Jaschke¹ in *Stoeckel's Handbuch der Gynäkologie* states that "ulceration, edema and perivaginal phlegmons may develop in a prolapse followed by purulent metro- and endometritis. The swelling may reach such a degree, the phlegmon may extend so rapidly to the rest of the cellular tissues that the prolapse, within a short time becomes irreducible." This author observed one case which spontaneously recovered through gangrene and sequestration of the major portion of the uterus. "In the majority of cases, however," he continues, "death results whether the patient is untreated, or an attempt to perform hysterectomy is made."

CASE REPORT

The patient was a 42-year-old, Irish housewife, para ii. Last pregnancy ten years ago. Prolapse of the uterus, always readily replaceable, existed for one year. For fourteen days preceding admission, the prolapse could not be reduced, confining the patient to bed. There was difficulty in micturition from the onset. No flatus or feces were expelled for the last two days.

She was admitted to the Gynecological Ward of Mount Sinai Hospital, the evening of Jan. 7, 1937. Temperature was 100.8° F., pulse 72, and blood pressure 100/80. The patient was thin, mental reactions were sluggish, and she was apparently not acutely ill. Abdomen was tympanitic and moderately distended. Inspection showed a huge mass protruding from and covering the vulva. The long diameter was 12 inches, transverse diameter 6 inches, and the circumference 19 inches. The mass was pineapple-shaped, being wider at midsection than at its base. The apex was formed by the huge, ulcerated and edematous cervix, the surface consisted of the everted vaginal mucosa, dry, scaly, with "bursting" ulcers in several areas. The color was deeply cyanotic, the consistence boggy, the percussion note posteriorly tympanitic. Pressure on the mass elicited gurgling. A catheter when passed entered the urethra and then pointed directly downward along the anterior surface of the prolapse. Rectal examination showed that posteriorly the rectal pouch was likewise eventrated into the prolapse (Fig. 1).

Sedimentation time was thirteen minutes, hemoglobin 75 per cent, and the urine normal.

During the first night attempts at reposition made by the resident, after the patient had been placed in steep Trendelenburg posture and warm compresses applied, failed. The following morning I failed in all efforts which included pressure on the apex both before and after applying a rubber Esmarch bandage.

Signs of intestinal obstruction: enemas ineffectual, increasing abdominal pain, distention, nausea, no flatus passed, as well as increase of the edema and cyanosis locally and poorer general condition, forced me to perform an abdominal section twenty-four hours after admission, repeated attempts at reposition having failed. Because of the local infection and the presence of much intestine in the prolapse, the vaginal approach was rejected.

While the patient remained in bed, the cervix remained high, at least 2 inches above the ischial spines. The vagina was gaping, only a vestige of perineum. On the forty-first day, a week after the patient had been up daily, a second degree prolapse developed but was readily replaced.

Fifty-seven days after the laparotomy a typical parametrial fixation operation² was performed by me. The cervix at this time measured $3\frac{1}{2}$ inches in diameter. The vaginal tissues and parametria were still edematous and boggy, the cervix of baconlike consistence. Convalescence was uneventful. Two and one-half months after this operation, conditions were found normal: cervix high, good perineum, and rather lax lateral walls. The patient is now fully cured for fourteen months.

The only case somewhat resembling the one I report, which I can find in the literature, and this patient did not survive, is one reported by Beyea³ in 1898. He called it "A Case of Acute Septic Infection and Strangulation of a Completely Prolapsed Uterus; Vaginal Hysterectomy; Death." This was a 22-year-old Irish para iv who had had a prolapse for six years. For the four previous years she was unable to reduce it, and for six days there were chills and fever, the temperature rising to 103° F. At this time, for three days there were distention and vomiting. Catharsis proved ineffectual. On admission to the hospital, the temperature was 101° F. There was no distention. Vomiting was constant. The pulse was 120. Beyea found the prolapse the size of a child's head, of reddish blue color, with 2 ulcers, each the size of a dollar. Calomel was given and the bowels moved 6 times in twelve hours. The urine was clear. His attempts at reposition were unsuccessful. The temperature was now 100° F., the pulse 112 to 116, the patient was weaker, and the mass more cyanotic. No distention had developed.

Beyea performed a vaginal hysterectomy, encountering intestinal loops, congested and covered with lymph. His examination of the uterus showed small, multiple abscesses in the myometrium. The patient died five days after operation with all the symptoms of diffuse peritonitis.

In the literature Baldy's⁴ case is frequently quoted in connection with Beyea's. Baldy's patient was seventy years old and found sudden enlargement of prolapse with pain and fever. The mass was twice as large as before. One-half of the mass showed ulceration and the entire prolapse was blackish in color. Baldy was able to reduce the prolapse completely after considerable difficulty. Seven days after the reduction he performed an abdominal operation (hysterectomy), there being fibroids present, fixation, and vaginal repair. This patient recovered.

Doubtless such cases as Slocum's⁵ occasionally occur without being reported. This was a negress of 47 years who had suffered from long existing prolapse, which suddenly became irreducible and produced pain. The prolapse was 7 inches long and 19 inches in circumference. Slocum saw it shortly after the acute symptoms developed, and after the patient had been in the knee chest position for one and one-half hours, he succeeded in reducing the prolapse by manipulation. This patient was kept in bed three days.

One of the reasons that irreducibility of prolapse is rarely encountered is due to the fact that unless an extremely sluggish and unintelligent patient suffers from this trouble, the symptoms are so acute and violent that immediate help is sought. In the early stages before stasis and edema have occurred, reduction should always be possible.

The present case has been reported in such detail, because it appears to be the only patient who survived the severe abdominal operation necessary, and because the previous reports are incomplete. It is also hoped to draw attention to the fact that early reposition and retention of the prolapse is essential in order to avoid more serious consequences.

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peritoneum of the right side of the pelvis had slid or been pulled down, carrying the caput coli and appendix to the bottom of the prolapse. The uterus could not be felt.

Under visual control from within, two assistants made continuous, concerted pressure on the prolapse from the outside below, occasionally relieved by a third physician; after twenty minutes, the inversion suddenly occurred, the entire mass passing through the vulvar ring and rising into the abdomen. The mass was edematous and so large that it projected inches above the incision. The collapsed cecum, the appendix, and the adherent terminal loop of the ileum could be readily

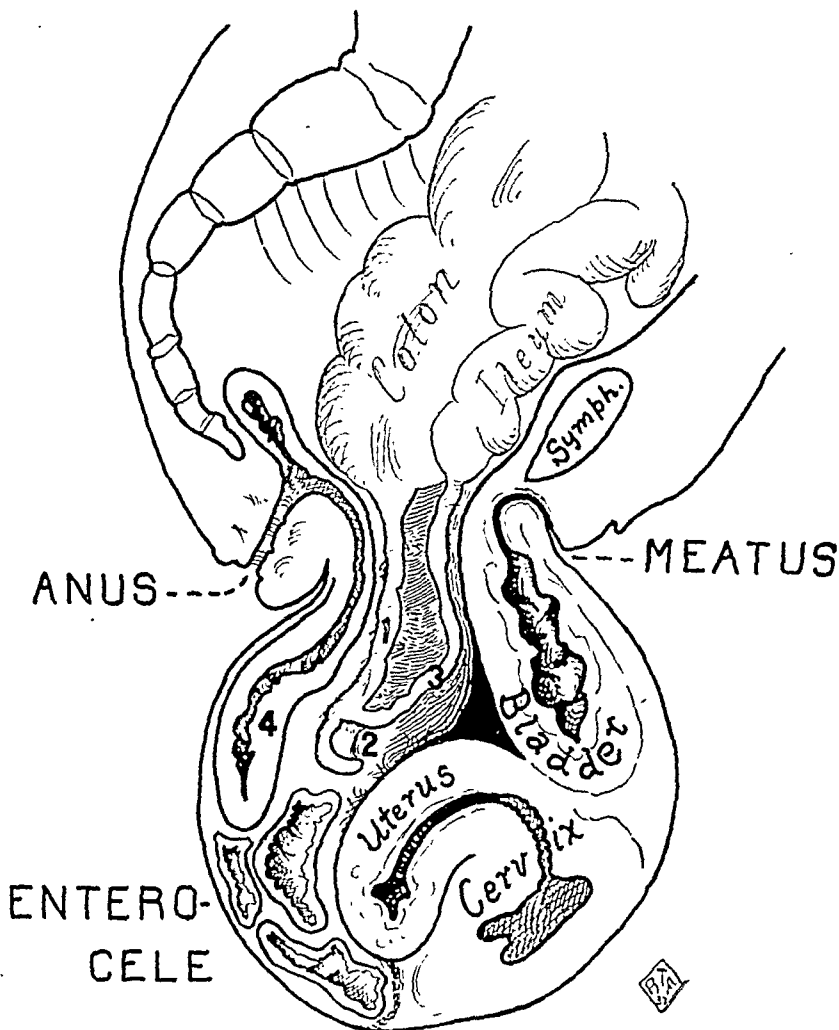


Fig. 2.—Schematic sagittal section through prolapse and pelvis. 1, Collapsed cecum; 2, appendix vermiformis; 3, terminal ileum; 4, lower rectum.

identified. The congested and thickened bladder likewise could be recognized but nothing of the uterus and adnexa could be seen because of adhesions. The abdominal wound was closed in layers with much difficulty, because of the excessive addition to the abdominal contents which overfilled the peritoneal cavity. Four laparotomy pads were packed into the vagina to prevent re-entrance of the prolapse.

The early postoperative course was stormy. Pneumonia and later a wound infection developed. After five days, however, the condition improved. The bowels moved spontaneously and the temperature fell. A tediously protracted, partly sub-facial infection of the abdominal wound prolonged the convalescence. For eighteen days a pack was kept in the vagina to keep the cervix at a high level.

At 4 P.M. she complained of being cold and of difficulty in breathing. The respiratory rate was 22 per minute. She stated that she had no pain. The blood pressure was again taken and found to be 88/68. The patient vomited dark brownish material, which upon examination gave a three-plus benzidine reaction. Examination at this time showed that the patient was pale and the skin cold. The abdomen was markedly distended but soft, and tympany was present in the epigastrium and in the flanks. No fluid wave could be demonstrated and no Murphy sign was present. The uterus was apparently larger than in the morning, now reaching a point about two finger breadths above the umbilicus. It was exquisitely tender throughout and firm but not rigid. The small tumor mass noted on the fundus at a previous examination was still present. No fetal heart could be heard and the position of the fetus was believed to be R.O.A. Vaginal examination failed to reveal any bleeding; the cervix was effaced and one finger dilated. The fetal head could be felt high up and appeared to be small and soft.

The pulse rate was 120, and the temperature was 95.8° F. Because of the drop in temperature and in blood pressure, rise in pulse rate, pallor, moderate air hunger and anemia, as revealed by the red cell count, it was apparent that concealed bleeding was occurring. Although the uterus did not present the typical ligneous feeling, it was believed that the patient was suffering from premature separation of the placenta with uteroplacental apoplexy and concealed hemorrhage, and that intra-uterine death of the fetus had occurred. Because of the bloody vomitus it was also considered that the bleeding might arise from some extra-uterine source such as peptic ulcer, but this was not thought to be probable in view of the absence of fluid in the flanks, the small quantities vomited, the negative previous history, and the localized uterine tenderness together with evidence of fetal death. It was advised that laparotomy be performed immediately together with transfusion.

Accordingly, under gas-oxygen-ether anesthesia, the abdomen was opened and was found to contain about 1,000 c.c. of fluid blood and an approximately equal amount in the form of a stringy clot which filled the left gutter. The uterus was enlarged to the size of a seven and one-half to eight months' pregnancy and on casual inspection appeared to be normal. By palpation a soft mass about 6 by 6 cm. was felt on the posterior surface of the uterus and was believed to be the lowermost portion of the clot mentioned. The source of the bleeding was not at once apparent. The uterus was emptied through a midline incision in order to permit more thorough exploration. When this was accomplished and a small stillborn female child delivered, the uterus was brought through the wound. On its posterior surface there was a jagged perforation 5 cm. in diameter, extending through the entire thickness of the wall. Through this opening collapsed membranes protruded, and it was then realized that the mass palpated before delivery consisted of these structures. The blood clot previously mentioned was adherent around the edges of the perforation and near by the left tube and ovary were densely adherent, evidently the result of a preceding inflammatory process. The right tube and ovary were normal. The left tube and the uterus were removed, the pelvis peritonized, and the abdomen closed. The patient was given 700 c.c. of whole blood by the direct method, without reaction.

The patient's postoperative course showed a marked reaction. The temperature rose within the first twelve hours to 101.6° F. and by the third day was 104° F. It remained at this level for three or four days, falling to 103° F., where it persisted until the eleventh day postpartum. Transfusion of 500 c.c. of blood was given eighteen hours after operation and again on the fifth postoperative day; numerous gum-glucose infusions were utilized. The blood pressure, which was unobtainable immediately after operation and for three hours thereafter was 126/96 at the fourth hour, and subsequently was approximately normal. Tachycardia was present and persisted for the first three days, frequently being timed at 150 per minute, but on the fourth day it found a level commensurate with the temperature, and then slowly dropped. The cause of the postoperative reaction was believed to be the large quantity of intraperitoneal blood, since at no time was there any evidence of infection and the wound healed by primary union. A blood culture taken on the fifth postoperative day was reported as containing a few colonies of *Staphylococcus aureus* (probably contaminant). Vaginal culture revealed gram-positive bacilli and cocci

ADENOMYOSIS IN A PRIMIPARA RESULTING IN SPONTANEOUS RUPTURE OF THE UTERUS AT THE ONSET OF LABOR*

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SPONTANEOUS rupture of the uterus in labor is a rare occurrence. Its incidence is variously estimated, but is probably in the proportion of about one case in 5,000 deliveries. DeLee¹ states that rupture is more often an accident among multiparas, and estimates that a ratio of 8:1 occurs in comparing multiparas with primiparas. A revised calculation of the frequency of spontaneous rupture of the uterus in primiparas appears to be about one case in 45,000 deliveries.

Most of the causes commonly assigned as responsible for spontaneous rupture of the uterus do not apply to the case here reported because they are based mainly on the theory that weakening of the uterine wall occurred as a result of frequent pregnancies or of previous operative procedures, such as myomectomy or curettage. Because it occurs so infrequently and because its pathogenesis is so interesting, the following case is recorded:

L. A., aged 25 years, colored, was admitted to the Bellevue Obstetrical Service at 8 A.M. Dec. 29, 1935, from another hospital. The patient had not attended a prenatal clinic. She stated that she was near term in her first pregnancy, the expected date being calculated as Jan. 6, 1936. She was awakened from sleep at 5 A.M. on the day of admission by pains recurring every five to ten minutes, lasting thirty seconds and not especially severe. For the past few weeks the patient said that she had to void urine about six times nightly, and on the morning of admission that she felt a continuous desire to empty the bladder.

Questioning failed to elicit any complaints other than the above. The patient denied any previous operation. The course of her pregnancy had been entirely uneventful.

Examination revealed a patient in good general condition. The pulse rate was 90 per minute, but the temperature was subnormal at 96.8° F. and later at 96.4° F. The blood pressure was 110/80. The heart and lungs were apparently normal. The abdominal examination revealed uterine and lower abdominal tenderness and some spasticity across the suprapubic region. The uterus was at the level of the umbilicus, a small firm projection being palpable at its upper pole. Fetal parts could not be outlined due to a fairly tense uterus, and several examiners were unable to hear the fetal heart. The patient insisted on lying on her side because it was painful to lie on her back. Rectal examination revealed a thick, closed cervix about 1 cm. in length. The presenting part was high and was believed to be a vertex.

Because of the urinary complaints and tenderness over the bladder region, the patient was immediately catheterized. The urine was cloudy, and contained innumerable polymorphonuclear leucocytes, and many small clumps of pus. The blood count revealed 23,800 W.B.C. with 86 per cent polymorphonuclear leucocytes and 2,710,000 R.B.C. with 60 per cent Hg. The blood was found to be Type 2.

A diagnosis was made of seven months' pregnancy with possible premature labor, and cystitis. The patient was given 2 gr. of sodium luminal to control pain. From this medication the patient became drowsy, slept at intervals, and did not complain greatly. The skin was cool and dry. The temperature 96.4° F.

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"In all sections throughout the musculature are seen clear areas lined by a thick layer of decidual tissue consisting of both compact and glandular layers of cells. (See Fig. 1.) This tissue is seen both close to the rupture and at a distance from it."

Diagnosis: Hyperplasia and edema of uterine musculature, rupture of the uterus, pedunculated subserous fibromyoma uteri, and adenomyosis uteri.

DISCUSSION

In the literature are reports of many ruptured uteri from a variety of causes. There are in addition many reports of adenomyosis. It seems strange that so few cases of rupture caused by adenomyosis should have been recorded. Marinacci² reports a case of rupture of the uterus following invasion of a cesarean scar by chorionic villi, that is similar to our case, but the cause of which is not so clear since two factors play a part. Aschheim³ mentions adenomyosis in a pregnant uterus with fibromyoma, as indeed do many others, but in Aschheim's case the pregnancy was not far advanced (about four months) and rupture did not occur. After a search of the literature only one case was found similar to the one here reported. The case in question was published by Richardson.⁴ Unfortunately no clinical history is given, the entire report being concerned with the pathologic findings in a case of spontaneous rupture of the uterus. The similarity of the two cases can best be appreciated by reference to the pathologic report, which is reproduced verbatim:

"Specimen is a uterus which had ruptured longitudinally on the anterior superior surface. The edges of the rupture are covered with a rough, dark red, friable material, apparently organizing blood clot, and section of the adjacent uterine wall shows an irregularly mottled red and white surface. No evidence of the scar of a former cesarean section is found. Microscopic sections taken at the edge of the rupture show uterine tissue with the characteristics of pregnancy. There is, in addition, a very considerable infiltration of the wall with decidual cells, extending deep into the muscle tissue. Some increase in connective tissue is also found. While it cannot be said that the infiltration was the cause of the rupture, the coincidence forces one to the belief that it was at least possible."

It is probable that the interpretation of Richardson's⁴ case in the light of the scanty knowledge of adenomyosis at the time of its publication, was somewhat different from the interpretation now generally accepted. Its title, "Ruptured Uterus With Decidual Cell Infiltration of Uterine Wall," seems to indicate that it was supposed that the invasion of the uterine wall took place after nidation owing to some abnormal stimulus to the cells themselves by pregnancy. With the current theories as to the pathogenesis of adenomyosis it becomes clear that the so-called invasion of the uterine wall is in reality the development of the changes of pregnancy in aberrant endometrium. This is supported by the findings, in our case, of numerous foci of decidual cells at a great distance from the endometrium and apparently having no direct connection with it, which connection, it must be supposed, would exist were direct invasion the pathogenetic factor. Further, the findings in cases of adenomyosis which are not complicated by pregnancy, seem to bear out this theory.

SUMMARY

An interesting and rare case of spontaneous rupture of a full-term primigravid uterus at the onset of labor is reported. The patient had had no previous operative manipulations of the uterus and by subsequent microscopic examination, and at operation it was demonstrated that adenomyosis was responsible for the rupture.

REFERENCES

- (1) *DeLee, Joseph:* (Quoted by Sheldon, C. P.) *AM. J. OBST. & GYNEC.* 31: 455, 1936. (2) *Marinacci, S.:* *Policlinico* 30: 921, 1923. (3) *Aschheim, Selmar:* *Arch. f. Gynäk.* 120: 303, 1923. (4) *Richardson, R.:* *Proc. Path. Soc. Phila.* 22: 53, 1919.

and gram-negative bacilli. No hemolytic microorganisms were present. The patient was discharged in good condition on the twenty-first postoperative day.

Pathologic Report.—(No. 4571/35.) The organs removed were examined macroscopically and histologically and the following report was given (Drs. W. E. Studdiford and H. Salter):

Macroscopic Examination: "Specimen consists of a uterus measuring 22 by 18 by 6 cm. The external surface is covered with a smooth pinkish-yellow serosa. Anteriorly there is a 6 inch surgical incision extending from the cervical to the fundal portion in the midline, the edges of which are approximated by catgut sutures. Posteriorly in the central fundal portion is a ragged, hemorrhagic perforation, which extends from serosa to endometrial surface. This opening is about 3 cm. in diameter. The tissue surrounding the opening appears similar to that of the rest of the uterus. On the left lateral aspect of the opening is the attachment of the round ligament to which is attached the folds of the broad ligament. The right round ligament is not present.

"On removal of the surgical sutures, the uterine walls are seen to measure 4 cm. anteriorly; posteriorly in the region of the above described defect, the musculature



Fig. 1.

measures 1.5 cm. in thickness and becomes thinned and more hemorrhagic toward the edges of the opening. The uterine cavity is lined by ragged, shaggy, pinkish-yellow tissue, stripping easily, which appears to be decidua. The interior of the uterine cavity near the perforation is striking in that there is a deep crevice in the tissue which measures 3-4 cm. in length and several mm. in depth, becoming deeper and broader as it approaches the inferior aspect of the opening with which it is continuous. There are several smaller crevices situated radially about the defect.

"On the anterior serosal aspect is a 2 cm. pedunculated tumor resembling a fibromyoma, the pedicle of which is 1 cm. in length."

Microscopic Examination: "Sections of the uterus show areas of smooth muscle cells formed into bundles and running at various angles. The muscle bundles, as well as the individual cells, are separated from each other by clear spaces appearing to contain fluid. The cytoplasm of the muscle cells is pale and shows many vacuoles. There appears to be a hyperplasia of the smooth muscle cells. The endometrial surface of the musculature is covered by decidual tissue consisting mostly of the glandular layer with no chorionic villi seen. There are also several large areas of old red blood cells in the tissue and areas of fibrin. A good many infiltrating polymorphonuclear leucocytes are seen in this latter tissue."

daily supplemented by 30 gr. of ammonium chloride in enteric coated tablets. Initial urinary pH was 5.9. By December 17, the temperature was normal, but clinically the patient showed only slight improvement. On December 19, chills, fever, nausea, and vomiting returned. Daily temperature ranged between 100 and 104° F. Although a urinary pH of 5.0 had been maintained since the beginning of treatment, the urine contained many pus cells and the Flexner organism was again isolated. Additional laboratory studies showed: blood chemistry within normal limits. Phenol-sulphonphthalein test showed 45 per cent excretion in one hour. Roentgenogram of abdomen revealed nothing abnormal. Retrograde urograms demonstrated bilateral dilatation of ureters and kidney pelves. Bromsulphalein liver function test showed 5 per cent retention in thirty minutes.

The management of this case was again carefully considered. The ketogenic diet was not applicable for a high carbohydrate, high caloric diet seemed indicated on account of high fever, loss of weight and strength, and evidence of beginning liver damage. In addition, there was anorexia, nausea, and vomiting. A ketogenic diet was, therefore, not practical. Therapeutic termination of pregnancy was considered. It was decided, however, to continue the mandelic acid therapy which was supplemented by ureteral catheterization and drainage of both kidney pelves, the latter being performed twice weekly. In addition, the patient received four blood transfusions of 350 c.c. of citrated blood.

On January 11, the patient developed an acute tracheobronchitis. Chest x-rays were negative for evidence of consolidation. Consultation with the General Medical Staff regarding the physical condition and with the Urologic Staff regarding the renal status, brought the recommendation of therapeutic termination of pregnancy as the final step to save the life of the patient.

The following day the membranes were ruptured. Labor followed eighteen hours later. Spontaneous delivery of a living, female child terminated an eight-hour labor. The child had not reached the age of viability and, consequently, lived but a few minutes. The placenta readily separated by the Schultz mechanism five minutes later. Estimated blood loss was 50 c.c.

Following delivery the temperature ranged between 100 to 102° F. for thirty hours but thereafter dropped quickly to normal limits where it remained during the subsequent nine days of hospitalization. The recovery was astounding. She immediately tolerated a full diet with a rapid gain of appetite, strength, weight, and showed general clinical improvement. Renal tenderness quickly diminished to slight residual soreness although the urine contained the Flexner organism and a moderate number of pus cells. Rapid improvement continued. When last seen in April, 1937, her general physical condition was excellent. She no longer presented symptoms referable to the urinary tract.

In a review of the literature, Calalb and Jonesco, in 1915, reported the first case of pyelitis due to the bacillus dysentery Flexner complicating pregnancy. They reported satisfactory results by treatment with autogenous vaccine.

Cheatham, in his case report with a review of the literature to 1934, cites only the case of Calalb and Jonesco. Cheatham's case was a multiparous woman in the seventh month of pregnancy complicated by pyelonephritis due to the Flexner organism. The patient spontaneously delivered a living female child of eight months. Profuse postpartum hemorrhage following the third stage of labor, indicated transfusion. With a very satisfactory convalescence, the temperature returned to normal by the seventh postpartum day. They were especially interested in the use of bacteriophage therapy which proved of little value. Vaccines were avoided because of the negative phase. Urinary antiseptics could not be used due to the unusual vomiting. The clinical value of mandelic acid therapy had not been recognized. They attribute the rapid improvement of their case to the use of postpartum blood transfusions.

PYELITIS OF PREGNANCY DUE TO THE BACILLUS DYSENTERY FLEXNER

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REPORTS of only two cases of pyelitis due to the Flexner type of dysentery bacillus complicating pregnancy have been published. The treatment was different in each case. In the case herewith presented mandelic acid was used. The ketogenic diet is also considered.

M. D., a white female, aged 20, was admitted to the Henry Ford Hospital Dec. 12, 1936. Chief complaints on admission were: pain in both kidney regions, generalized abdominal pain, persistent nausea and vomiting, frequency of urination, dysuria, loss of weight and strength. All symptoms were present three and one-half weeks. The last menstrual period was July 15, 1936. The estimated duration of pregnancy was five months. Occasional backache, frequency of urination, and dysuria were first noted at the end of the second month of pregnancy. Independent of treatment, a slight temporary improvement of symptoms was present until the beginning of the fourth month when pain and dysuria returned with greater severity. This was soon followed by chills, fever, generalized abdominal distress, nausea and vomiting. Within the next week, she was confined to bed with persistent vomiting, loss of weight, abdominal pain, chills, fever, and extreme weakness which continued until admission to the hospital.

The family history is irrelevant. The past history is not significant. Appendectomy was performed at the age of thirteen with an uneventful recovery, otherwise, she never had symptoms referable to the gastrointestinal tract and claimed good general health.

Positive findings on physical examination were: temperature 104.4° F., pulse 156, respirations 24, blood pressure 96/50. The patient appeared very toxic and the dry skin presented evidence of dehydration. She was 20 pounds underweight. The face was thin and drawn. Mucous membranes were pale. Dental caries was present. Tongue was coated and dry. Lungs were clear. Heart was normal. Fundus of uterus extended 15 cm. above the symphysis pubis. Fetal movements were seen and felt. No other organs or masses were palpable. There was generalized abdominal tenderness as well as extreme tenderness in both costovertebral angles. She was critically ill.

Laboratory findings were: Hemoglobin, 60 per cent; R.B.C., 3,050,000; W.B.C., 22,000 with 87 per cent polymorphonuclears and 13 per cent lymphocytes. Catheterized urine showed specific gravity 1.020, acid reaction, trace of albumin, many pus cells, occasional red blood cell, no casts and tests for sugar, acetone and diacetic acid were negative. Centrifuged specimen: stained sediment showed many pus cells and many Gram-negative bacilli, identified as the Flexner bacillus of dysentery. Patient's serum agglutinated the Flexner bacillus in a dilution of 1:640 but was negative for the typhoid-paratyphoid groups. Stool cultures were negative for dysentery organisms. Blood chemistry showed: CO₂, 44.7 vols. per cent; non-protein nitrogen, 22.0; chlorides, 450. Blood serology negative.

Because she was unable to retain fluids by mouth, parenteral fluids were forced for the first thirty-six hours of hospitalization. Two days after admission, she tolerated a liquid diet. Mandelic acid therapy was instituted by giving 12 gm.

of amenorrhea which lasted six months and again her weight increased. During this time she suffered severe headaches and developed a hypertensive state. Following thyroid medication for her obesity, her headaches became less severe and her menses reappeared but in irregular fashion.

Present Illness.—For two years prior to her admission to the hospital her menses were infrequent and scanty. She was free from symptoms until two months before her admission when her menses recurred. The flow at this time lasted seven days and was accompanied by intense stabbing pains in the lower part of the back, the right lower quadrant, the thighs and calves of the legs. After an interval of two days she again began to bleed. This bleeding lasted another seven days and was accompanied by similar pains. From then and continuing to the time of admission, she bled every other week. This was accompanied by severe abdominal pains, headaches, dizziness, nausea, blurring of vision, and chills. There was no change in the urinary or bowel habitus.

Physical Examination.—Revealed a very obese, plethoric woman, who seemed at ease and not acutely ill. The heart was enlarged to the left and right, and a soft blowing systolic murmur, which was not transmitted, was heard at the apex. The blood pressure was 180 systolic and 100 diastolic. The abdomen disclosed a thick panniculus arranged in large folds which hung down to the knees. On deep palpation, indefinable masses were felt in both lower quadrants of the abdomen. Both ankles were markedly swollen and there were numerous varicose veins on both legs. Pelvic examination: revealed a lacerated pelvic floor and cervix; a movable, very tender and semicystic mass was palpated in the cul-de-sac which, by bimanual examination, extended to four fingerbreadths below the umbilicus; another large mass was palpated more anteriorly on the right. A diagnosis of bilateral ovarian cysts was made. The laboratory data were as follows: the blood sugar content was 192 mg. per 100 c.c. of blood; the Wassermann and Kahn tests were negative; urinalysis was repeatedly negative. The blood count showed over 5 million red blood cells, hemoglobin 74 per cent (Dare), white blood cells 12,800, with 74 per cent polymorphonuclear neutrophilic leucocytes, 21 per cent lymphocytes, 4 per cent monocytes, and 1 per cent eosinophiles.

Operation.—On Feb. 5, 1935, under spinal anesthesia, the abdomen was opened through a lower paramedian incision. Bilateral ovarian cysts were exposed. The right was nodular and appeared dermoid in character. It was as large as a good sized grapefruit, with half a twist of the pedicle, but freely movable in the pelvis. The round ligament was adherent to it. The cyst on the left was about half the size of the one on the right and situated behind the uterus in the cul-de-sac. It likewise appeared to be a dermoid. The uterus, lying between both cysts, was small. A supracervical hysterectomy and bilateral salpingo-oophorectomy was performed and the cervical stump peritonized. An appendectomy was also performed. During convalescence, the temperature remained normal with a rise to 101.6° F. on one occasion. The blood pressure gradually declined to 130 systolic and 80 diastolic. She recovered uneventfully and was discharged on Feb. 26, 1935, three weeks postoperative.

Pathologic Report.—The specimens consisted of the appendix, the uterus, tubes, and bilateral ovarian tumors. The uterus and tubes appeared normal. The surface of the appendix appeared smooth and gray, and the mucosa and muscular wall were normal. The smaller of the two ovarian tumors was spherical and measured 8 cm. in diameter. The surface was smooth and gray pink. The contents consisted of thick, yellow, butterlike material intermixed with hair. A small mass present in one portion of the cyst was incorporated in the wall and when sectioned consisted of osseous and adipose tissue. The larger tumor (Fig. 1) measured 16 cm. in diameter. The contents resembled that of the smaller tumor, with a large amount of thick, yellow, opaque, mucinous material. A pedunculated bean-shaped mass attached by one pole to the inner surface of the cyst, consisted of a central mass of red tissue surrounded by yellow fatty tissue. In another part of the wall was an irregular swelling which projected in the form of several nodules which were hard, yellow and pink, and appeared to be bone.

In our case, vaccines and bacteriophage were not given a trial for we relied upon the use of mandelic acid combined with adequate renal drainage. Mandelic acid treatment of pyelitis of pregnancy due to the colon bacillus has been very satisfactory, but in this case it did not affect the Flexner organism. Several blood transfusions were given prior to therapeutic induction of labor without appreciable results, which is not in accord with the experience of Cheatham. Furthermore, the postpartum course of our patient showed a rapid cessation of all symptoms independent of blood transfusions and specific medication to the urinary tract. A further contrast to Cheatham's case was the absence of postpartum hemorrhage.

SUMMARY AND CONCLUSIONS

A rare case of pyelitis of pregnancy due to the bacillus dysentery Flexner is reported. The organism was isolated from the urine on several occasions and identified by the usual cultural characteristics. The organism was agglutinated by known antiserum. The patient's serum agglutinated the Flexner bacillus in dilutions 1:640 but was negative for typhoid-paratyphoid and other dysentery organisms. Stool cultures were negative for Flexner bacillus.

Mandelic acid therapy alone and later supplemented by adequate drainage of kidney pelvises proved unsatisfactory in this case in contrast to experience with pyelitis of pregnancy due to the *Escherichia coli*.

In view of the severity of the infection and the clinical course prior to therapeutic induction of labor, the ketogenic diet was contraindicated for the patient.

On the recommendation of two consultants, pregnancy was terminated, which proved to be a lifesaving procedure for the mother. Postpartum convalescence was rapid and independent of treatment; therefore, any form of therapy during this time must not be regarded as specific.

BILATERAL OVARIAN DERMOID CYSTS

WITH ONE DERMOID CONTAINING AN APPENDIX AND A PORTION OF ILEUM

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THE following case is unique as a pathologic rarity and worthy of record.

K. S., a housewife, aged 39, was admitted on Feb. 1, 1935 to the Gynecological Service of Dr. Leo S. Schwartz at the Jewish Hospital of Brooklyn with the following history:

She complained of severe pain in the right lower part of the back and intermittent vaginal bleeding of two months' duration. Family history was irrelevant. Past history: married fifteen years, gravida iii, para ii, and one miscarriage at four months. She had frequent attacks of dyspnea on exertion with mild cyanosis and ankle edema. The history of her weight development coincident with her menstrual history revealed a definite endocrine influence. During the stage of puberty she was a puny girl. At 25 years she weighed 145 pounds; five years later her weight increased to 200 pounds. At the time of her admission to the hospital she weighed 225 pounds. Her maximum weight was 243 pounds. Her menses had always been irregular and were accompanied by premenstrual pains. At 26 years she had a period of amenorrhea during which her weight reached 222 pounds. With a proper diet her weight decreased to 160 pounds, after which her menstrual periods again recurred at intervals of two and three months. At 37 years she had another period

Microscopic.—The uterus, tubes, and appendix showed no pathologic changes. A variety of tissues was recognized in both tumors: viz. bone, muscle, and fat. A section of the appendiceal structure, lying within the cyst (Fig. 2), revealed the various layers of the appendix. The mucosa was intact, and the submucosa contained several immature and one mature lymph follicles. The muscular coat and the serosa were well formed. The lumen contained débris, mucinous material, and a few cells.

Diagnosis.—Bilateral dermoid cysts of the ovaries.

PLACENTA ACCRETA

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MRS. L. P., a white American multipara, aged 31 years, was admitted on my services at Dallas Methodist Hospital, Sept. 2, 1936. Her first pregnancy was normal in all respects; she delivered an 8-pound girl on Sept. 12, 1933. On the present occasion she started labor at 5 A.M. and entered the hospital at 6 A.M. She was in first stage of labor, having pains every five minutes, duration one minute, and a cervix effacing with 2 cm. dilatation. At 9 A.M. pains were every two minutes and lasting one minute. At 10:30 A.M. the cervix was completely dilated. One hour later midforceps were applied, and a normal live 9 pound girl baby was delivered. Thirty minutes later the placenta had not delivered, and Credé's method was unsuccessful. A short mediolateral episiotomy was repaired. Because the placenta would not be expelled under normal methods, it was decided to keep the patient on the delivery table, taking all precautions against infection. The cord with forceps clamped on one end was wrapped in a sterile towel and laid on the abdomen. 1,000 c.c. of 5 per cent glucose was given intravenously, also $\frac{1}{4}$ gr. of morphine. Later examination revealed that the uterus remained stationary in the abdomen, and the placenta could be palpated in the fundus. There was no flow, no rise of the globular fundus uteri, and no descent of the cord. The patient was in good condition. A diagnosis of placenta accreta was made without an intrauterine examination. The patient was prepared for operation while donors for a blood transfusion were obtained. She had been asleep since 9 A.M. under nembutal. At operation a supravaginal hysterectomy and appendectomy were performed. Immediately after the operation the patient was given 470 c.c. of whole blood by the direct method. The patient was in good condition when removed to her room. The temperature went up to 100° F. for two days, after which it was normal. The next day after operation, the patient said she felt fine and believed she could get up. She made an uneventful recovery and was discharged from the hospital on the eighth postoperative day.

The patient was given her final examination January, 1937, some four months after the delivery. She stated at that time that she had had no aches or pains, or any nervous symptoms. Examination revealed a healed perineum and normal pelvic organs. She was discharged as well.

On opening the uterus after operation the placenta was normal to look at except that there was no separation from its attachment in the fundus of the uterus between both cornu. No line of cleavage for separation could be made manually. The pathologic report made by Dr. J. L. Goforth is as follows:

Gross Examination.—The supracervical portion of the uterus was symmetrically enlarged and measured approximately 14 by 12 by 12 cm. A few scattered fibrous adhesions were present about the posterior portion. On being opened the myometrium showed much hypertrophy. The endometrial cavity contained a term-

On further dissection of the large dermoid, another compartment was disclosed, and the wall which separated this from the main cyst cavity was markedly thickened. In the smaller loculus was a segment of intestine 14 cm. long and 3 cm. in



Fig. 1.—Gross specimen. *A*, Appendix in cyst; *B*, small intestine in cyst; *C*, cut edge of smaller cyst compartment; *D*, grumous material; *E*, hair; *F*, cut edge of large cyst proper.

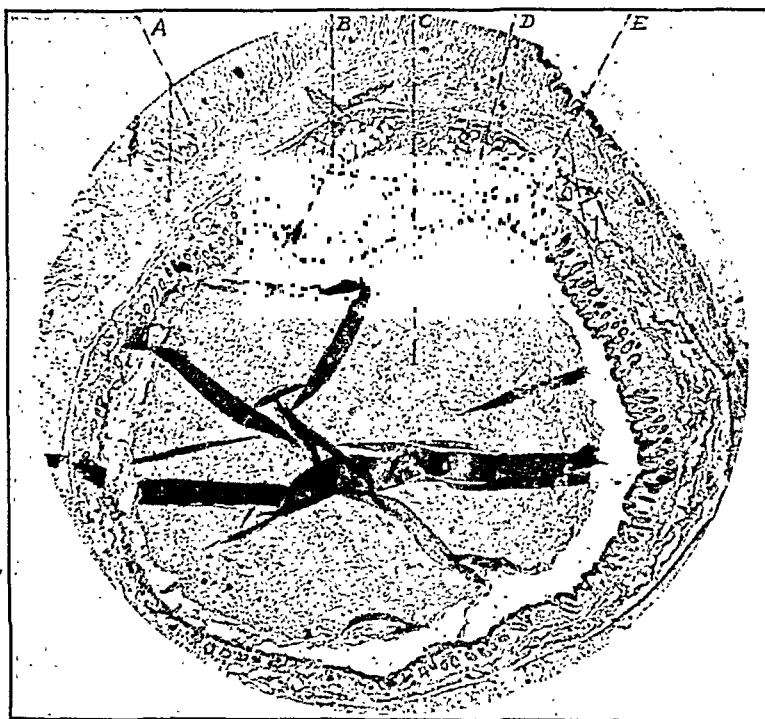


Fig. 2.—Gross specimen of appendix within cyst. *A*, Muscular layer; *B*, lymph follicles; *C*, cellular and amorphous debris in lumen of appendix; *D*, submucosa; *E*, mucosa with mucosal glands and tubules.

diameter. One-half the length of this intestine had the appearance of ileum, and the other half, the caliber of which was much narrower, closely resembled a vermiform appendix with a rudimentary mesentery attached.

CEREBRAL COMPLICATIONS FOLLOWING NITROUS OXIDE ANESTHESIA

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DURING the past few years several articles in the literature have presented cases showing evidence of nervous tissue damage following nitrous oxide anesthesia. Most authors have believed the injury due to anoxemia; a few have suggested that idiosyncrasy may play a part. We feel unentitled to a definite belief in the two or more sides of this controversy. The articles by Courville¹ and by Löwenberg and others² with the bibliographies of each are references aplenty for those interested. Our own case follows fairly well those already published.

An 18-year-old para 0, gravida iii was admitted to the hospital in labor at 8:45 P.M. on Jan. 15, 1937. Her prenatal record showed a normal pregnancy. On admission blood pressure was 120/80, presentation was cephalic, and station was -1.

At 11 P.M. 1/6 gr. of morphine and 1/150 gr. of scopolamine were given. At 1:30 A.M. she was taken to the birth-room apparently well sedated. N₂O and O₂ anesthesia was begun by the interne on anesthesia service at 1:40 A.M. Her pulse was 124, respiration 20. Induction required 92 per cent N₂O and 8 per cent O₂, was rather slow. During the following eight minutes N₂O concentration varied between 92 per cent and 80 per cent. At 1:48, following episiotomy, a normal, slightly narcotized infant was delivered by means of low forceps. The patient was awakened, talked freely, named her baby, and appeared normal in every way.

Ergotrate gr. 1/320 was given intravenously, the placenta delivered at 1:58 A.M.; anesthesia again was induced with about 92 per cent N₂O, and continued with about a 9:1 gas-oxygen ratio. During the ensuing minutes respiration became slow, shallow, and labored on two occasions, each time responding quickly to an increase in O₂. At 2:20 A.M., about twenty-two minutes after the second induction, respiration became labored, irregular, did not respond to 100 per cent O₂, and finally ceased altogether. The patient became markedly cyanotic, the pupils dilating widely, the eyeballs fixing in the central position. On administration of 100 per cent O₂ under pressure the patient's color returned, but respiration was gasping, irregular, and very slow. The pupils were contracted. The tongue at no time seemed to obstruct the pharynx, but an air-way was inserted and tolerated. Metrazol, an analgesic, 1 c.c. was given intramuscularly at 2:26 A.M. and repeated intravenously at 2:39 without immediate benefit to respiration. A small amount of vaginal bleeding was noted and 1 c.c. of pituitrin was given intramuscularly. At 3:15 the pulse was 150, the blood pressure 180/80, respiration 15, and the rectal temperature 100°. Oxygen 100 per cent was discontinued, but of necessity resumed immediately, small amounts of CO₂ being added. Eyeball movements were active; the lid reflex returned. The patient seemed conscious, but did not respond to her surroundings nor to ordinary stimuli. By 3:28 A.M. respiration, though still irregular, seemed of better quality, rate 28. At 3:40, 1 c.c. of metrazol was given intravenously; ten minutes later respiration was regular and deeper. Blood pressure was 130/90. At 3:55 it was found that O₂-CO₂ were no longer necessary. At 3:30 reflexes had been found to be very sluggish, but at 4:00 A.M. the patient began to show a spasm of the upper extremities similar to carpopedal spasm. All reflexes became active. Seizures developed and were repeated every five to ten minutes, characterized by movement of the head from side

sized placenta which measured 14 by 14 by 13 cm. This organ was so tightly adherent to the uterine wall that it could not be pulled away. The fetal surface, cord, and fetal membranes grossly were not remarkable. On section through the placenta an unusually firm union between placenta and uterine wall appeared to exist. On gross study it could not be determined with certainty whether the decidua basalis was present or not. The placental tissue itself showed no degenerative changes grossly. Throughout the body of the organ localized hemorrhagic areas 1 to 2 cm. in diameter were demonstrable. The myometrium from the gross point of view could not be said to be invaded by placental tissue.

Microscopic Examination.—Sections through different portions of the placenta, the sections being taken so as to show both placenta and myometrial tissue, showed that the chorionic villi were normally firm. The muscle fibers of the myometrium



Fig. 1.—Section of tissue showing the absence of decidua basalis and invasion of the myometrium by chorionic villi.

were tremendously hypertrophied. There was practically no decidua basalis tissue between the placenta and myometrium. Here and there a small irregular patch of decidual cells was noted but a decidual layer could not be made out. The myometrium was moderately well invaded by chorionic villi. From the microscopic point of view this invasion was sufficiently well established to account for the adherence of the placenta to the uterine wall in terms of nonseparation. The sections revealed no evidence of malignancy and the invasion described did not extend very deeply into the myometrium. Here and there the myometrium itself seemed to peninsulate into the placental tissue. The union between the placenta and myometrium was usually firm at these sites.

Pathologic Diagnosis.—Postpartum uterus with adherent placenta (placenta accreta).

Operation.—Lower median incision into the peritoneal cavity revealed some free blood. In the entire lower abdomen and extending above the umbilicus were numerous large fibroids as large as full-term fetal heads. The left tube was compressed between a large fibroid and lateral wall of the pelvis. Upon freeing the tube there was a rent in its outer third, between the isthmal and ampullar portion from which protruded a fetus and placenta. The left tube was removed, leaving the left ovary.

UNUSUALLY LARGE MULTIPLE FIBROMYOMATA OF UTERUS
COMPLICATING RUPTURED EXTRAUTERINE PREGNANCY

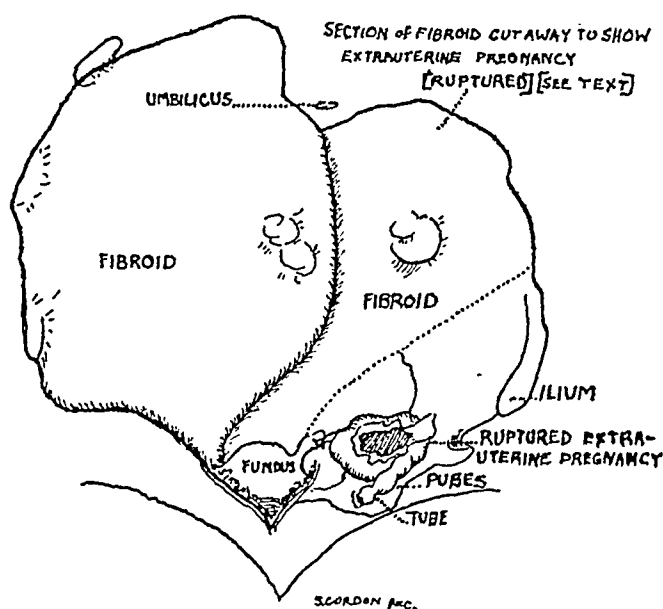


Fig. 1.

Nothing else was done. The abdomen was closed without drainage, and the patient made an uneventful recovery, and will return at a future date for a hysterectomy.

Comment.—The compression of the left tube between one of the fibroids and the lateral wall of the pelvis accounted for the small amount of free blood in the peritoneal cavity and, consequently, the patient's not showing marked signs of internal hemorrhage.

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Hudson, Alfred E. A.: A New Technic for the Examination of *Trichomonas Vaginalis*, *Malayan M. J.* 12: 73, 1937.

A simple method of demonstrating the *Trichomonas vaginalis* consists in obtaining a drop of vaginal secretion by means of a pipette or medicine dropper and placing it on a warm slide, on which is a drop of warm saline solution. The protozoan parasites, if present, will be recognized by their rapid, jerky motions, swimming to and fro. Dark-field examination is not necessary.

Various morphologic types have been described by Goddall: pineapple, wind-mill, angler, spin-wheel and the seal. Mixed types are not usually found in the same case.

F. L. ADAIR AND S. A. PEARL.

to side, flexion of both arms with carpal spasm, marked spasticity of both lower extremities with bilateral Babinski phenomenon, and a wide frightened expression in the eyes. There were some clonic movements of the upper extremities. Mild opisthotonus was present at intervals. The patient was returned to bed at 5:30 A.M. where she soon became so wild and noisy that sedation was necessary. At 11 A.M., Jan. 16, 1937, the temperature was 102°, pulse 140, and respirations 22 to 44.

Neurologic and neurosurgical consultation gave an impression of "diffuse cortical and basal ganglion cell injury." The patient's neurologic condition changed but little until death on Feb. 5, 1937. Temperature at death was 106.8° F. per rectum.

Treatment had included morphine, 10 per cent and 20 per cent intravenous glucose, parathyroid hormone and calcium levulinate intravenously, resulting in transient improvements. Oropharyngeal O₂ was used for a few days when pneumonia threatened on Jan. 26. Feeding by stomach tube was necessary throughout most of the illness. Incontinence was the rule. Autopsy was not permitted. Urinalysis, blood counts, blood chemistry, and spinal puncture were all essentially negative through the postpartum course.

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RUPTURED EXTRAUTERINE PREGNANCY COMPLICATING UNUSUALLY LARGE MULTIPLE FIBROIDS OF UTERUS

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RUPTURED extrauterine pregnancy is occasionally seen associated with small fibroids, usually solitary, of the uterus, but a case seen in conjunction with large multiple fibromas is worthy of reporting.

M. R., negress, aged 32 years, no children, with a history of one pregnancy years ago terminating in a three months' spontaneous abortion, was admitted to the gynecologic service of Dr. Wm. Gauch at the Newark City Hospital, with pain in the lower abdomen and an amenorrhea of two months' duration as her chief complaint. The patient was first seen in consultation with the Medical Service of the hospital, to which service the patient was originally admitted for a supposed respiratory disorder; the diagnosis of an acute surgical abdomen was made, and laparotomy was decided upon.

Physical Examination.—Well-developed negress, apparently in acute pain, centered in lower portion of abdomen; temperature 100, pulse 90, respiration 22; blood pressure, 132/80; W.B.C., 9,850, polymorphonuclears, 86 per cent; R.B.C., 3,800,000; Hg, 55 per cent; urinalysis essentially negative.

Head and chest showed no pathology.

Abdomen: Tenderness and some rigidity over entire lower abdomen; large multiple fibroids felt, one extending to three fingerbreadths above the umbilicus on the right, and on the left large nodules extending to the umbilicus and completely filling the pelvis.

Vaginal Examination.—Perineum not relaxed, cervix soft, numerous large fibroids completely filling the pelvis and extending upward above the umbilicus, no tenderness in the fornices.

Rectal Examination.—Confirmed vaginal examination.

6:00 A.M. feeding and noticed that it could not move its right leg. She took it in to the mother for nursing, and at 7:00 A.M. she called the interne. He found the right leg to be fractured in the middle third of the femur. Upon my arrival in the hospital at 9:00 A.M. I found the leg was broken. An x-ray was ordered and Fig. 1 shows the right femur fractured at the middle one-third, the proximal fragment overriding anteriorly. The condition of the other bones in the body was normal.

Upon close questioning of the night nurses and the supervisor on duty in the nursery, it was found that the baby was not handled from the 10:00 P.M. feeding until it was taken up in the early morning. The baby had not been dropped nor roughly handled, and there were no signs of external trauma nor any discoloration anywhere on the body. No hematoma was found on the leg, nor any evidence of hemorrhage or violence.

The leg was then placed over the abdomen and chest, and bandaged in position. At the end of fourteen days, union had taken place, as noted by x-ray, so that the leg was removed from its restriction. The fracture occurred on June 29, and the last x-ray, Fig. 2, taken in September, 1936, shows the leg to be in accurate alignment.

The mother of this baby was given 60 gr. of calcium daily throughout the pregnancy and the nursing period. She also had vitamin A, B, D capsules. There was no evidence that the intake of calcium was insufficient for herself and the baby. According to the dentist's report, her teeth remained in good condition.

On checking the literature, I was unable to find anything that had a direct bearing on the case, except that in 1933 Dr. Bercovici reported a case somewhat similar. A brief abstract follows:

"It was a case of double fracture of both femurs. The x-ray showed an oblique fracture situated at the junction of the middle and upper thirds of each femur. The bones seemed to be more permeable to the rays. There was no injury which could have caused the fracture of these bones."

There is no family history of fractures in Bercovici's report, nor is there in mine. Bercovici reports 5 other cases in abstract. In 2 of these, fractured femurs occurred at the time of birth, and a few days later, fracture of the arm occurred. In 3 cases the fractures were noticed after the child was two or more years of age. In these cases it is evident that the children were suffering from "Lobstein's disease." In 1833, Lobstein described the condition by characterizing it as "an idiopathic form of brittle bones without demonstrable local lesions." Eddowes, in 1900, published a paper calling attention "to the peculiar blue sclerotics appearing synchronously with the bone lesions, and suggesting that they hold a place of importance in the symptom complex of osteopsathyrosis."

The baby in our case had no evidence of Lobstein's disease.

In the Chicago area I was able to locate another patient who had multiple spontaneous fractures occurring after birth. The fractures also occurred on different days. This case is to be reported.

SPONTANEOUS FRACTURE OF THE FEMUR IN THE NEONATAL PERIOD

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SPONTANEOUS fractures which occur in the neonatal period are sufficiently rare to warrant reporting a case. A young woman, 28 years of age, reported in her third month of pregnancy. At that time nothing abnormal was noted. Her family history was non-essential, as were her previous illnesses. The Wassermann and Kahn tests were negative, and the blood count was within the normal. She reported



Fig. 1.



Fig. 2.

Fig. 1.—Fracture of the femur as seen by x-ray, June 29, 1936.

Fig. 2.—Fracture of the femur as seen by x-ray, Sept. 10, 1936.

to the office regularly at the usual prenatal intervals. There was no finding of significance, except that she had gained more weight than the average patient. The highest blood pressure reading during pregnancy was 120/70; the urinalysis was normal.

She entered labor spontaneously one day after the menstrual due date. After twenty-one hours in the first stage of labor, she delivered spontaneously, having a forty-five-minute second stage of labor. The baby, a female, was perfectly normal, weighing 3170 gm. The baby nursed and was given supplementary feedings. The patient was to be discharged on the twelfth day.

On the evening of the eleventh day, the baby was taken to the mother for its 10 o'clock feeding and was in excellent condition. It was placed in the crib, and nothing wrong was noticed by the night nurse until about 5:00 A.M., when she heard the baby cry loudly. She picked the baby up at that time to prepare it for the

part of pregnancy, but from the beginning of labor to the end of the second stage. Schluter⁵ clearly emphasizes that the fetal heart tones be observed after each pain during the latter part of the second stage of labor. This should save more babies.

The old type of the head stethoscope is not more generally used, partly because of the failure of any one instrument to properly fit all heads and ears. I have designed a new model which is so adaptable that it will fit any wearer, thus eliminating the only objection to the instrument as a part of the equipment of the delivery room. It is hoped that the new model will facilitate and encourage the general use of the head stethoscope in obstetrics, including home as well as hospital deliveries. This stethoscope, which has been satisfactorily employed at the Prenatal Clinic and birth rooms of the Cook County Hospital for the past year, presents the following advantages: (1) The head band is adjustable to any head. (2) The ear pieces are adjustable to fit all ears. (3) This stethoscope may be worn comfortably for hours. (4) Fetal heart tones can be heard through only one ear piece, if desired. (5) The bell may be sterilized with the same solution as used on the skin. (6) It offers a clear field of vision since the rubber tubing is elevated to the head band. (7) As the rubber tubing is elevated and approximated to the bell stem, it reduces the possibilities of contaminating the sterile field when listening to heart tones. (8) During a forceps operation the long bell stem may be flexed temporarily upward out of the way. (9) Because of the thumbscrew-operated joint at the base of the bell stem, the stem may be easily adjusted to a more favorable angle.

I gratefully acknowledge the suggestions and cooperation of Dr. David S. Hillis in the designing of this instrument.

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30 NORTH MICHIGAN AVENUE

Bager, B.: Is the Sedimentation Reaction of Any Practical Importance in Complications During the Puerperium? Acta obst. et gynec. Scandinav. 16: 387, 1936.

The author investigated Fahraeus' sedimentation reaction in 401 women immediately before and one week after delivery with a view to finding out whether this reaction is of any value for estimating complications arising during the puerperium. About half the number of cases were normal and the other half were pathologic. The physiologic variations in the sedimentation reaction proved to be exceedingly great and capricious, both as regards the value obtained before delivery and its increase or decrease during the puerperium. Among the pathologic cases the sedimentation reaction was also shown to vary considerably. The author concludes that the sedimentation reaction is practically of no value during the first week of the puerperium even with a control value immediately before delivery for comparison.

J. P. GREENHILL.

NEW MODEL HEAD STETHOSCOPE

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TWENTY years ago Hillis¹ introduced for the first time the head stethoscope. The purpose of this instrument was to hear plainly the fetal heart tones and to facilitate their counting during labor without the aid of an assistant and without contaminating the sterile gloves and gown. A few months later DeLee² introduced

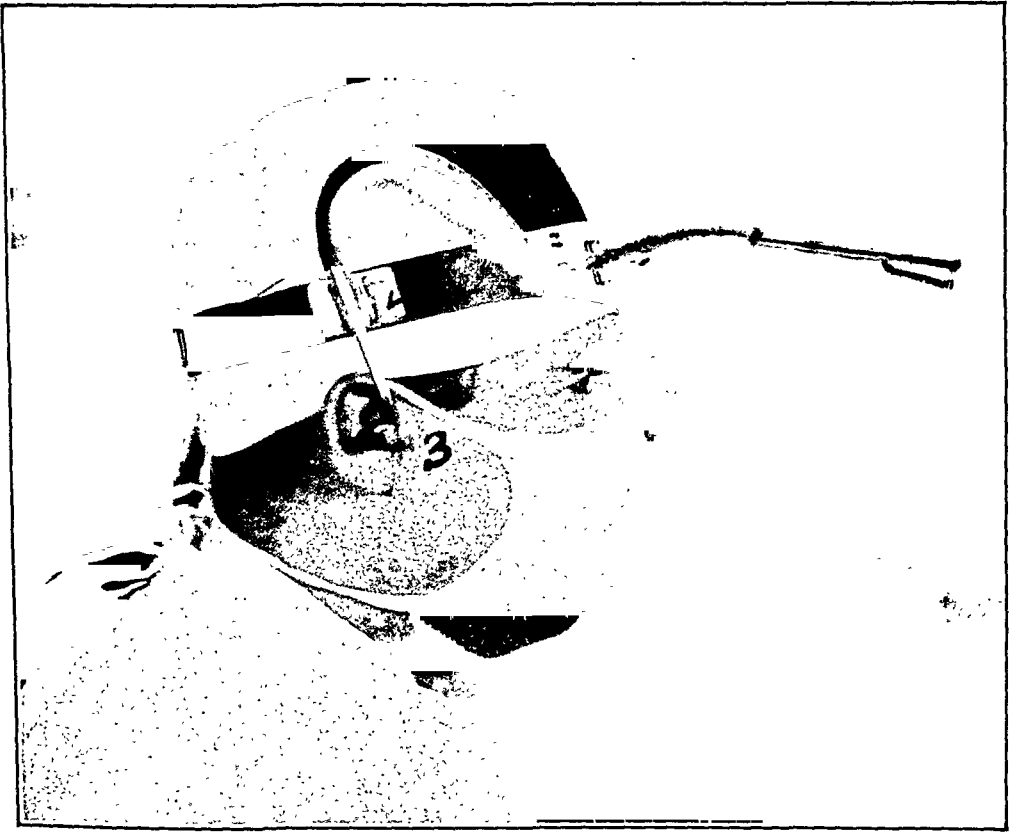


Fig. 1.—1, Bell stem which is two and one-half inches longer than old type. 2, Thumb screw for flexion or deflexion of bell stem. 3, Ear piece. 4, Attachment for ear piece by universal joint, allowing the following movements, upward, downward, forward, backward, inward, and outward. The inward and outward movements are controlled by a simple spring which causes the ear tips to snugly fit the ears. 5, Clamp for adjustability of headband, with special control. 6, Clamp to keep tubing above the line of vision.

a head stethoscope with minor changes. In 1922, Falls and Hunter³ added a watch and mirror to the stethoscope, a feature that aided in accurately counting the fetal heart tones. In 1923, Falls and Rockwood⁴ designed the microphonic stethoscope amplifying the fetal heart tones sufficiently to be heard by the unaided ear a few feet from the loud speaker.

If the head stethoscope fits the head and ears it is an invaluable instrument during labor and particularly during the latter part of the second stage. An ill-fitting stethoscope is an annoyance and cannot be used with comfort or success. It is of greatest importance that the fetal heart tones be observed not only during the latter

obstetrician, he owes it to his patients and to the cause of medical progress generally to examine this problem carefully, and to take whatever steps he can toward diminishing its seriousness.

It is hardly necessary here to spend time on the phrase "psychosis of pregnancy." Obstetricians and psychiatrists alike, throughout the literature, have pointed out that there is no circumscribed mental picture that may be ascribed to reproduction. The old notion that pregnancy provides a specific etiologic agent in the production of mental disease has, I believe, been laid by the heels. It will suffice to say that the psychoses associated with reproduction appear in all of the temporal phases of the reproductive cycle, that the clinical pictures may simulate practically any of the psychoses found in nonpregnant women, and that the prognosis varies also. There is, then, no "psychosis of pregnancy." But when we recall the 9 per cent contribution of pregnancy to the total psychoses in females, and in the light of the fact that the incidence of psychoses among pregnant women is almost twice that among the female population generally, we cannot but feel that pregnancy and its implications may provide distorting influences that are more intense than women are ordinarily called upon to face. But inevitably, the question arises: why do not added stresses and strains affect all women alike? The endocrinologic, metabolic, and cardiovascular alterations of pregnancy have come to be looked upon as physiologic. Why, then, do some react to them differently than do others? The conscious notions regarding the ordeals of pregnancy and the rearing of children are, for the most part, fairly well standardized. Why should the gross emotional response of one woman to this situation vary so markedly from that of her neighbor?

The answer to these questions often is difficult to find in any specific case. When one examines the problem generally, however, the explanation is more apparent. If you will permit me to digress somewhat for a moment, I will summarize briefly the pluralistic approach to psychiatric problems. We may consider the individual, for purposes of this discussion, as having been in the beginning a mass of formless but malleable clay. What, then, were the influences which molded her into this finished product with which we, as physicians, have to deal? How did she evolve into this person with her particular physical set-up and personality? A detailed exposition of the phenomena involved would necessitate an entire series of lectures. We can, however, briefly classify the molding forces into four crude groups.

There are, first, the constitutional factors which result in the individual's native endowment, and which are derived from hereditary, intra-uterine, and infantile physical influences. Next may be mentioned the factors which make for personality development—early environment and experiences plus training—which establish the emotional pattern of the individual and set up potential reactions, both desirable and otherwise, that may manifest themselves at any time during the life span, depending on the circumstances in which the individual finds herself. Third are the physical inroads of disease which may occur at any time, and which may alter the individual's capacity for adjustment either by direct action on one or the other of her tissues and organs, or by limiting or distorting her perspective and thereby making for emotional changes. The fourth, but by no means least important, group of stresses and strains are those incident to the attaining of maturity, which necessitates an assumption of

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

PSYCHOSES COMPLICATING CHILDBEARING

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THE incidence of psychoses associated with childbearing has been given by various writers on the subject as ranging from 1 in 400 to 1 in 1,192. The average of the different ratios cited for Queen Charlotte's Hospital, the Rotunda Hospital in Dublin, Ireland generally, and listed by DeForest, Langdon, Frumkes, Armstrong-Jones, and Partridge is 1 in 858. In other words, of every 858 women who enter the cycle of reproduction, one is likely to become psychotic during the period beginning with conception and ending with lactation. On first thought one might be inclined to dismiss this ratio as being so small as to depict a possibility which need cause little concern. After all, a percentage incidence of slightly more than 0.1 per cent is hardly great enough to merit consideration!

We will, nevertheless, pause for a moment of consideration. In the first place these figures represent, for the most part, only those patients who are sufficiently abnormal mentally to have been noticed by the non-psychiatric observer. In the second place, a good many of the so-called psychotic developments of pregnancy do not manifest themselves until some time after delivery, so that the connection may not be recognized. As a result of these two factors, many of the less spectacular mental states and a number of those which develop postpartum probably do not contribute to the ratio I have given. Consequently, the percentage incidence probably may be assumed to be higher than 0.1 per cent.

Let us view the situation from a somewhat different angle. Cole says that 7.5 per cent of all female psychoses are associated with reproduction. DeLee places the figure at 10 to 18 per cent. The State of New York attributes 3 or 4 per cent of its total female state hospital admissions to childbearing. Zilboorg reports that of 10,000 psychotic women, the psychoses were incidental to pregnancy and its sequelae in 8.7 per cent. Stone and Karnosh found a similar association in 5.5 per cent of 1,604 psychotic women. If we roughly average these percentages, we obtain a result of 8.9 per cent. It may be said, then, that of all females who suffer from psychoses of various sorts, almost 9 per cent develop their mental disorders in connection with the reproductive experience. That 9 per cent, it seems to me, places a problem squarely in the laps of obstetricians. Since an appreciable proportion of the psychotic female population develops its mental disturbances while under the observation of the

the time and expense involved in the lengthy preparation for his work. A six months' apprenticeship in an active maternity hospital would have equipped him adequately for the mechanical performance of his duties. Fortunately, however, most obstetricians are assuming the responsibilities that are properly theirs as physicians. Their interest is no longer focused exclusively on the pelvis, with the result that the metabolic and endocrinologic activities during reproduction are becoming progressively more understandable to all of us. Their consideration of the emotional implications of pregnancy, however, has not kept pace with these other advances. It is necessary that obstetrics include in its armamentarium a greater measure of psychiatric understanding. Therein rests a large part of the prophylaxis against not only the psychoses, but also the much more frequent, less intense emotional disturbances that evolve from pregnancy.

Reviewing the available English literature on the subject which has appeared during approximately the past twenty-five years, a total of 946 cases was found. It is to be regretted that the facts regarding these cases that were selected for tabulation were not discoverable in every instance. The accumulated results, nevertheless, may have some instructive value.

The literature conforms, for the most part, to the custom of classifying the types of psychoses which are associated with pregnancy into three major divisions: schizophrenic, manic-depressive, and toxic-exhaustive. Though the clinical pictures seen frequently are likely to be more or less atypical, this classification is in the main acceptable, and is particularly useful from the point of view of prognosis. In addition, most writers on the subject attempt to group their cases on the basis of the phase of the reproductive cycle in which the psychosis first was apparent. Robinson, as a result of a questionnaire submitted to a number of psychiatrists, found the consensus of opinion to be that the temporal divisions are three: the period of pregnancy, the puerperium (including the first six weeks postpartum), and the lactation period (after the sixth week postpartum). Zilboorg, in this connection, states that 15 per cent of the cases occur during pregnancy, 25 per cent during lactation, and 60 per cent during the puerperium. In our own survey, which included 770 cases concerning which this information was available, 24 per cent occurred during pregnancy and 76 per cent had their onset postpartum. Of the postpartum cases, the psychoses began within the first two weeks in 80 per cent, with lactation period contributing only 4 per cent. Precise information regarding the time of onset in the pregnancy cases was listed in only 22 instances, of which 16 occurred in the third trimester. This corresponds to the generally advanced statement that of those psychoses which begin during pregnancy, the majority first become manifest in the later months.

Concerning the diagnostic incidence, it was not possible in this survey to obtain an adequate differentiation between the schizophrenic and manic-depressive cases; so that our classification includes both of these groups under the functional division, and compares them as a unit to the toxic-exhaustive cases. The latter are reported variously as comprising 32 per cent to 48 per cent of the total psychoses. Of 891 cases in our survey, 35 per cent were toxic-exhaustive and 65 per cent functional. It is felt generally that the percentage of functional psychoses is likely to be higher among the prenatal cases than among those developing postnatally; whereas the toxic-exhaustive incidence climbs postpartum.

independence, an acceptance of responsibilities, an active participation in a competitive existence, and so on.

These are the forces, past and present, which determine the individual's ability to adjust, and which color the mental picture that she presents. Each force, in itself, is made up of a complexity of possible factors; and the interaction of all of them in different individuals may make for a diversity of personalities and reactions which is only to be compared to the total number of individuals existent. When, in attempting to understand the dynamics of a given mental picture, we take into account all of these factors, we are employing the pluralistic approach. There is no other intelligent manner of handling psychiatric problems—or, for that matter, medical problems generally. We must consider always the total picture that the patient presents, and resist the temptation to relax into the error of dealing with a pathologic finding as though it were a thing apart from the remainder of the individual. The psychobiologic unit that we call man always includes, is dependent upon, and reacts as a unit to all of its functions, normal and otherwise.

Pregnancy, involution, and lactation are usually regarded as physiologic processes. The facts that women are predisposed structurally to these phenomena, and that they are reared in an environment which tends to condition them psychologically to accept maternity as a matter of course, would seem to remove the stigma of pathology from the picture. In the larger biologic sense, also, the perpetuation of the species could hardly be called pathologic. And the apparent truth that the vast majority of women reproduce without mishap attests to the normalcy of the entire affair. Despite these facts, however, we must not forget that pregnancy and its sequelae do bring about profound, even though transient, physical and chemical changes in the individual. And in addition, the mental experience of childbearing and its multitude of possible emotional ramifications is hardly to be regarded as negligible. We have in reproduction, then, the superimposition on the woman of stresses which, even though they may be considered part of her physiologic and psychologic heritage, are nevertheless representative of a load that is greater than she is accustomed to carrying. When we add to this the increased possibilities for actual physical disturbance, infection, hemorrhage, thrombosis, and so on, the possible load becomes even heavier. Thinking pluralistically, we should not be surprised if some of the many possible weak links in the personality occasionally break under these added strains. It is true that there is no "psychosis of pregnancy." But pregnancy may well provide, in a variety of ways, the precipitant that will crystallize an existing potential departure from the normal.

The answer, then, to the question, "Why do some women react differently to the experience of reproduction than do others?" is apparent. Not all women are alike, either physically or in regard to personality makeup. I realize, of course, that this is no startling disclosure, and that all of you are aware of it. What is surprising, however, is the ease with which this more or less obvious fact is forgotten or neglected. The problem of the psychoses that develop in association with pregnancy is, from the practical point of view, no more a matter for purely specialized psychiatric solution than are cardiac deliria or disturbances in mental equilibrium secondary to nutritional deficiencies. The obstetrician who limits himself to an urinalysis prenatally, the delivery of the infant, and the removal of an episiotomy suture postnatally, might have spared himself

Strecker and Ebaugh found in their material some suggestion that Jewish women are more susceptible to severe mental upset as a concomitant of the childbearing experience than are women of the other religious groups. I was not able to find any other data or opinions concerning the existence of racial or religious differences in this matter. McGoogan stresses the importance, as predisposing factors, of previous pregnancy experiences and of heredity. Crowder feels that hypo-ovarianism holds grave prognostic possibilities.

Regarding the significance of the presence of hereditary taint, the literature covered by this survey was again inadequate. Reference to the presence or absence of markedly abnormal mental findings in the ancestries of these cases was not made in a large number. From those reports which included this information, 163 cases with definite pathology in the family tree were found. Considered against the background of the total number, these make up 17 per cent. It is quite probable that with complete historical information in every instance, this percentage would be appreciably higher. Despite the fact that this degree of incidence of hereditary findings is significant statistically, the usual difficulties encountered in trying to evaluate hereditary influences generally are present here also. Perhaps the most honest attitude would be to view a patient's poor heredity with suspicion, but to avoid allowing it in itself to play too prominent a part in the coloring of predictions regarding the course in any given case.

A possible contributing circumstance that has been given a good deal of consideration is illegitimacy. The additional affective stress that is the usual complement of illegitimacy, plus the probability that illegitimate pregnancies are more likely to occur in women who are, to begin with, less well-adjusted emotionally, intellectually, and financially, would seem to make it likely that this unconventional factor identifies a group which has a greater chance of becoming psychotic during the reproductive period than have more conforming women. Partridge states flatly that the percentage incidence of psychoses associated with illegitimate pregnancies is greater than one finds in married cases. Armstrong-Jones says that of all the cases he could find, 12 per cent were illegitimate. The latter compares this figure to the smaller total incidence of illegitimate births in the population generally, and deduces that the discrepancy can only mean that illegitimacy is a definite factor in the production of psychoses. He points out, also, that most of the psychoses in these cases occur before delivery. This, from the purely psychogenic point of view, should not be difficult to understand; and in addition, the comparatively high incidence of psychoses among illegitimate cases should eliminate any doubt that might exist regarding the ability of psychogenic factors to produce mental upheavals.

The problem of infanticide has earned some comment in the literature. Ricksher says that it is rare. Hopwood found that of all murders committed by female psychotics generally, 25 per cent were instances of infanticide. He states that these crimes occurred for the most part during the lactation period. McIlroy, investigating statistics at the Criminal Lunatic Asylum at Broadmoor for the period from 1900 to 1924, found that 42.8 per cent of the admissions were for child murders in connection with psychoses associated with pregnancy. She, too, points out the higher incidence during lactation, and is inclined to blame the psychoses

Of 808 cases, 60 per cent were multiparae and 40 per cent primiparae. Most statistics agree that multiparae show a greater total of psychoses than do primiparae; and the deduction that is usually drawn from these figures is that any given multipara pregnancy is more likely to be complicated by a psychosis than is a first reproductive experience. Indeed, psychologic reasons why this should be so have been advanced. I would like to point out merely that there are more multipara than primipara pregnancies; and that this fact alone may well provide the explanation for the greater number of multipara psychotics. As a matter of fact, it would not be surprising if complete data would show that the percentage incidence of psychoses is actually higher in primipara pregnancies. The unusual physiologic changes, the alterations in physical appearance, the anticipation of the ordeals of parturition, the magnification of the responsibilities of maternity generally, and the crystallization of unconscious emotional potentialities all probably contribute to making the first experience an especially difficult one mentally. In this connection, one probability worth mentioning is that psychoses seem more likely to develop during pregnancy in primiparae, and postpartum in multiparae.

It is impossible, without more data than were available, to draw any significant conclusions from the age incidence of this series of cases. The average age was thirty years, with 46 per cent occurring between the ages of thirty-one and thirty-five, and the group from twenty-six to thirty years contributing 32 per cent. A large majority of the psychoses, then, developed between the ages of twenty-six and thirty-five; but this span corresponds to the period of greatest fecundity, which dilutes the significance of the finding.

Regarding the presence or absence in the patients' histories of psychotic episodes previous to the pregnancy under observation, positive information was recorded in only 196 cases, with 81 having had psychoses with previous pregnancies, 40 not associated with pregnancy, and 75 concerning whom no mention was made as to whether or not the psychoses were coincident with reproduction. Taken as a group, these 196 comprise 20 per cent of the total; and if we assume that the actual incidence of previous psychoses would be even higher with adequate data regarding all the cases, this factor presents itself as a probably significant premonitory warning. This statement is qualified because no figures on the past histories of a control group of uncomplicated pregnancies are at hand.

An attempt to discover pertinent material regarding the prepsychotic personalities of these cases was disappointingly unproductive. Zilboorg asserts that aloofness, frigidity, chronic masturbation, homosexual trends of more than ordinary intensity, and long courtship are frequent findings in the histories, particularly of those individuals who develop the schizophrenic type of reaction. Bernard Glueck agrees with Zilboorg, and adds as predisposing qualities the schizoid personality make-up, eccentric or extremist notions regarding sexual matters in any direction, and difficulty in sharing one's self between parents and husband. Anderson, comparing these factors in psychoses associated with pregnancy to those independent of reproduction, found no significant difference in the two groups. It seems plausible that the findings of Glueck and Zilboorg hold potentialities for psychopathology regardless of whether the precipitating strain be pregnancy or something else overly strenuous physically or emotionally. Davidson does not feel that frigidity is a particularly decisive force in the causation of the psychoses under discussion.

raculous suddenness at the time the uterus empties itself. Except for an occasional toxic case, where the toxicity apparently is dependent specifically on the pregnant state, the regression of the mental abnormalities usually may be expected to be gradual. The intervention of death in these patients is more properly a function of the physical than the mental condition; though in the toxic cases particularly, the superimposition of exhaustion secondary to excitement or malnutrition is likely, of course, to accentuate the gravity of whatever somatic disorder may be present. It is in the toxic group that most of the fatalities occur. Regarding the mortality among the children born to women who are psychotic during pregnancy itself, Ricksher finds the rate to be high. To recapitulate briefly, then, the prognosis generally may be considered good, even in psychoses of relatively long duration. This is especially true among those women whose prepsychotic personalities and adjustments were adequate.

Wherein, now, may the obstetrician look for possible danger signals in his patients? Some of the more frequently occurring immediate premonitory manifestations are evidences of general discontent on the part of the patient, emotional changes in the direction of either depression or excitement, increasing tension, excessive anxiety, apprehension, and agitation. The introduction into the picture of marked irritability, suspiciousness, the development of phobias, and personality changes generally should cause the physician to be on his guard. Insomnia is often an ominous sign, as is the development of physical exhaustion. Fairly frequently the first sign of an oncoming mental upheaval is a newly developed concern over trivialities; and increasing garrulousness is felt by some authors to be particularly significant.

In addition there are the more remote, but nevertheless important, factors which always bear investigation from the point of view of anticipating a mental break. First and foremost, of course, are the general physical condition of the patient, and her physiologic ability to withstand the rigors of reproduction. The course of the pregnancy, the severity of the labor, and the efficiency of the involution and other postpartum phenomena hold possibilities for upset. The expectant mother's observable emotional reaction to childbearing and its various implications merits consideration. It is important to discover, if possible, how apprehensive she is regarding pain, and how courageous she usually is in the face of discomfort. The existence of a schizoid personality, and particularly the history of previous "nervous breakdowns" are warnings that should not be neglected. Unsuccessful attempts at abortion, in addition to the possible physical sequelae, frequently result in conscious and unconscious guilt feelings that may play havoc with the patient subsequently. The factor of illegitimacy may be disturbing. The general characteristics of the patient's environment and her attitude toward it, her adjustment to her husband and his reaction to her pregnancy, her degree of emotional maturity, her intellectual capacity, the economic problems that she must face because of the expansion of her family—all these details, and more, need to be considered in estimating the patient's mental capacity for adjustment to the various stresses of reproduction.

The obstetrician, if he is to do his patient justice, must bear all these things in mind. It is not nearly enough to become thoroughly acquainted with the pelvic outlet. He, in common with all physicians, must view

on the occurrence of physical and mental exhaustion in undernourished and overworked women. According to McIlroy, depressions are more frequent than excitements in the lactation period. With the patient farther removed from parturition, and consequently more likely to have discontinued medical care; and with the depression not so likely to stimulate close observation on the part of the family as is the more spectacular excitement of the earlier psychosis, the opportunities for infanticide are accordingly enhanced. It would be well to point out at this time also that inadequate observation likewise increases the chances for suicide in these patients, as it does in all mental cases. Despite the tendency in some quarters to consider child-murder a rarity, Langdon's feeling that every psychotic woman who has a child should be considered potentially infanticidal merits judicious incorporation into the attitude of the physician who handles such a case. Certainly with this attitude the chances for infanticide will be diminished. The reminder by Morton, who points out that not every infanticide is an indication of insanity, should be remembered, particularly when the legal aspects of these cases are being considered.

Concerning the outlook in the cases under discussion, it is generally agreed that the prognosis may be considered good in most instances. Figures given by various clinicians range from 76 per cent to 53 per cent recoveries. Of 719 cases in this survey (deaths not included) concerning whom the outcome could be determined, 65 per cent terminated favorably. It is well to keep in mind that a large proportion of these cases were state hospital patients, and therefore could be assumed to represent the least favorable prognostically. The outlook, consequently, probably may be considered even more optimistic than these figures indicate. Of 283 recovered cases in which the duration of the disease was determinable, the psychosis lasted less than one month in five, from one to three months in 49, from three to six months in 110, from six to twelve months in 81, and more than a year in 38. Thirteen patients remained psychotic for approximately eight years each, and then recovered. If these 13, who distort the total picture unduly, are eliminated, the average duration of the psychosis in these 283 cases was six months. It was not possible in this survey to attempt an estimate of the prognosis in the light of the time of onset of the psychoses. It is probable, however, that predictability in cases of this sort is more properly dependent on the type of mental reaction that occurs than it is on the time of occurrence. In this connection, James says that 96 to 97 per cent of the manic-depressive cases may be expected to recover from any given attack, with recurrences, of course, quite possible; that the outlook in the toxic cases is excellent if the physical pathology can be overcome; and that the schizophrenic types offer the worst prognosis. He points out that even though the psychosis persists for as long as a year, recovery may still take place. Even though the schizophrenic reactions present the least favorable possibilities, the prognosis in these cases should be considered definitely better than in schizophrenia generally. Concerning the time of occurrence some writers have felt that, with regard to the postpartum cases, the seriousness of the prognosis increases with the lengthening of the interval between delivery and the onset of the psychosis.

There exists in many quarters something akin to a superstition that psychoses occurring during pregnancy are likely to disappear with mi-

Editorial

The Physician as Practical Eugenist

AS POPULATION experts elucidate the statistical intricacies of the differential birth rate, and while the biologists pile up the evidence of gene responsibility for many of the excellencies and inferiorities of mankind, the general public is beginning to lose its traditional confidence in haphazard breeding of children.

The physician finds himself very much "on the spot." He is again as on many previous occasions of his long travel from individual towards social medicine, at a sort of crossroads with the professional sign board giving him equivocal directions.

Shall he keep to his original job of treating the sick and leave to the sociologist, the journalist, the geneticist, the promoter of general welfare at large, to translate into public understanding and personal conduct the lessons of human biology?

Shall he shoulder a new undertaking and prove that he is practically as well as etymologically a *Doctor*?

It would be contrary to good precedent and an evidence of professional retrogression if the physician of today did not meet the challenge of the instant need with the courage bred of knowledge.

Such resources as society can control will inadvertently, or, with good or evil intent, be used to impair or improve the physical and mental qualities of future generations. It is the study of such agencies, such forces and tendencies of society which constitutes eugenics.

In this the physician has an ever deepening concern and cannot long escape a professional decision as to his overt action in the matter of particular families or prospective parents, or of the premarital couples who must or wish to seek his aid in an intelligent way of married life.

The questions may be as blunt as "To marry or not," "If marriage, then what?," "Shall we have children, and probably what kind?," "Will you help me, or us, to mate and so breed as to offend neither the offspring, nor the society of our time and later?"

What the physician can contribute is perhaps little in amount, but in quality big with potentialities. He can reach another and more critical level of interest on his spiral stairway of preventive medicine. Having established the necessity and value of prenatal care he pushes back the threshold of his concern into the preconceptive choice of marriage conduct, and further still into the elements of choice that may prevent or determine marriage.

* * *

The physician must always consider himself the direct inheritor and personal employer of all sound biologic knowledge for human ends. He

his patient as a psychobiologic unit, the different constituents of which are intimately interrelated, the cardiac efficiency with the intrauterine nutrition, the endocrine activity with the circulatory tension, the psyche with the soma. Not only the major psychoses, but also the less intense maladjustments which may make for a much greater total of unhappiness, might well be avoided in large part if more obstetricians interested themselves in the complete personal and physical lives, past and present, of their patients. Whether, as Bernard Glueck has put it, the patient is possessed of psychobiologic fitness for marriage should be of primary concern; knowing this involves, of course, an expenditure of time, frequently, considerable time. The patient has a right to expect this sort of interest from her doctor. If his conscience does not force him to investigate his cases from every angle, and to measure emotional potentialities and repair mental trauma as he does pelvic diameters and perineal tears, he is only half a physician. The psychiatrist can help, of course. In the majority of cases, however, properly interested management on the part of the obstetrician will eliminate the need for specialized psychiatric aid.

There has been a definite effort made, during the past decade especially, to anticipate mental and emotional difficulties through an alliance between pediatricians and psychiatrists. It seems to me that we might well begin our prophylactic approach at an even earlier developmental level. If we want well-adjusted children, we must strive for emotionally efficient motherhood. To the obstetrician is given the opportunity for preparing the way.

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about 300,000 cases a year, some go to hospitals where expert obstetric anesthetists are not provided, others are attended in their own homes, or in nursing homes by the general practitioner (and our nursing homes sometimes leave much to be desired). Only a very small proportion, one might say a negligible proportion, of women in England are attended by a skilled obstetrician accompanied by a skilled anesthetist.

At one time the difficulties indeed seemed insurmountable and would have been insurmountable, had it not been for the unremitting efforts of a body of lay people led by Lady Baldwin and Lady Rhys Williams, who formed "The National Birthday Trust Fund" to provide money so that research work might be done in order to find some way by which all women could be given at least some relief in their labors. A start was made with chloroform in the form of chloroform capsules. These chloroform capsules are small crushable glass ampoules containing 20 minims of chloroform, and are crushed and placed in a mask which is held two inches from the patient's face when in pain.

Very good results were obtained and permission was sought from the appropriate authorities for their general use.

The British College of Obstetrics and Gynaecology carried out a test of chloroform administered by various methods to see whether the required permission ought to be granted, but they came to the conclusion, with considerable regret they said, that in considering the results of chloroform analgesia the conclusion was reached: that the administration of chloroform in any form or by any method carried with it a danger of death.

It was evident then that chloroform is not the agent for which we so earnestly sought.

Nitrous oxide and oxygen was considered impracticable because it was thought that that apparatus was too expensive for everyday use, too difficult to carry about, and that its administration could not be placed in the hands of midwives.

In 1933, however, a great advance was made. Dr. Minnitt, an anesthetist of Liverpool, suggested using a mixture of nitrous oxide in air instead of nitrous oxide and oxygen, of such strength that from its inhalation, no patient would be fully anesthetized. Dr. Minnitt found that when nitrous oxide was inhaled, a period of insensitiveness to pain was experienced before consciousness was lost, and he described this condition as analgesia.

He used an automatic apparatus for the administration so that all the patient had to do was to breathe in and out from a rubber facepiece, laying the facepiece on one side when the pain passed away, and the flow of gas was automatically shut off.

Dr. Minnitt's method was taken up enthusiastically by the "National Birthday Trust Fund" which paid all expenses for an official investigation of his technique by the British College of Obstetrics and Gynaecology. The College came to the conclusion that the administration of gas and air by the Minnitt apparatus was not associated with any increase in the risk of death in childbirth, that the method did not involve any added risk to the fetus, that the actual administration did not call for any more special skill than that which might be required by a midwife during her period of training, and that relief from pain was obtained in a high percentage of cases.

They also found that the administration of gas and air carried with it no remote risk to the baby, and that the method had no deterrent influence on the natural course of labor.

The Central Midwives Board have now altered their regulations to enable midwives to administer gas and air analgesia to their own patients.

At the Wellhouse Hospital, Barnet, and at the British Hospital for Mothers and Babies, Woolwich, we have used gas and air analgesia for all our cases and are well satisfied with the results. We do not obtain painless labor because we do not start our administration of gas and air until there is some prospect of delivery taking place, and we make no attempt to render the patient unconscious.

For primiparas, we usually start the administration when the cervix is nearly fully dilated, and for multiparas, when the cervix is dilated to the size of a 5

will receive, and as a student of medicine should demand, an increasing breadth of instruction on the social and individual implication of eugenics. As he takes his clinical histories he will surely be more than ever inquisitive as to the factors of inheritance.

He will encourage the requirement of premarital medical review of prospective parents, more for avoiding genetic than syphilitic catastrophes. He will inform himself on, and share with his patients, the safe techniques which may spare the parents humiliation and the inevitable sorrows of mismating.

He will teach the precious privilege and high degree of safety of normal maternity for the wholly fit.

He will take part in efforts for reversal of dysgenic tendencies which threaten to wreck nations as well as the family, by learning and then practicing eugenics through teaching the principles of racial progress.

Haven Emerson, M.D.

Correspondence

Gas and Air Analgesia

To the Editor:

In this country we are greatly indebted to American anesthetists for their pioneer work in analgesia and anesthesia in labor, and the article in the November number of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* by Dr. Arthur Bill is of great importance. Anesthetists will be envious of the splendid results obtained.

Dr. Bill mentions the bitter opposition to proposals for the relief of pain which is still not altogether uncommon and I think that, with us, this opposition arises for three reasons. (1) Many practitioners fear that the general demand of analgesia in labor will greatly add to their work and their difficulties; (2) the bad results obtained, as Dr. Bill says, due to bad judgment or bad technique; and (3) the bad results obtained from an attempt to conduct every labor entirely painlessly.

Many practitioners believe that if there is a general demand from women for relief from the pains of childbirth, they will be called upon to spend many hours at the bedside of their patients administering an anesthetic, and there is a very real fear on the part of the overanxious practitioner that the administration of analgesia and anesthesia in labor often leads to premature interference with the normal process of labor, and it may have a bad effect on both mother and child.

This fear is not entirely groundless, because there is evidence today that, in an attempt to produce absolutely painless labor, we can kill by kindness.

In his article, Dr. Bill brings out very clearly what are the general difficulties standing in the way of any attempt to relieve all the pains of labor for all women. "Clever administration of the general anesthetic is really the most important part of the conduct of painless labor," he says; and we all know how few in number are the clever administrators. In conclusion, he tells us it must be assumed that for conducting the type of labor described by himself, there must be adequate facilities, so often found only in hospitals. In the discussion which followed Dr. Bill's paper, other practitioners bring out the same difficulties.

These are just the difficulties with which we have been faced in this country for many years. Here, about one-half of the total confinements are conducted by midwives in the patients' own homes without the presence of a doctor. Of the remainder,

The patient should clearly understand exactly what to expect, she must be told that she will not lose all sense of consciousness and that she will not lose all sense of feeling. She must be persuaded to cooperate, and here we realize the importance of not making the patient too sleepy with sedatives in the early stages of labor, because the importance of the cooperation of the patient cannot be overestimated.

The patient must be told to apply the facepiece of the apparatus firmly to her face and to breathe deeply in and out as long as the pain lasts, laying the facepiece aside when the pain passes away. When she comes to the pushing down stage of labor, the patient must be told to take 4 or 5 deep breaths of gas, hold her breath and push, then 4 or 5 more deep breaths, hold her breath, and push again. When the baby is actually being born, we administer continuous gas and air, and after about 30

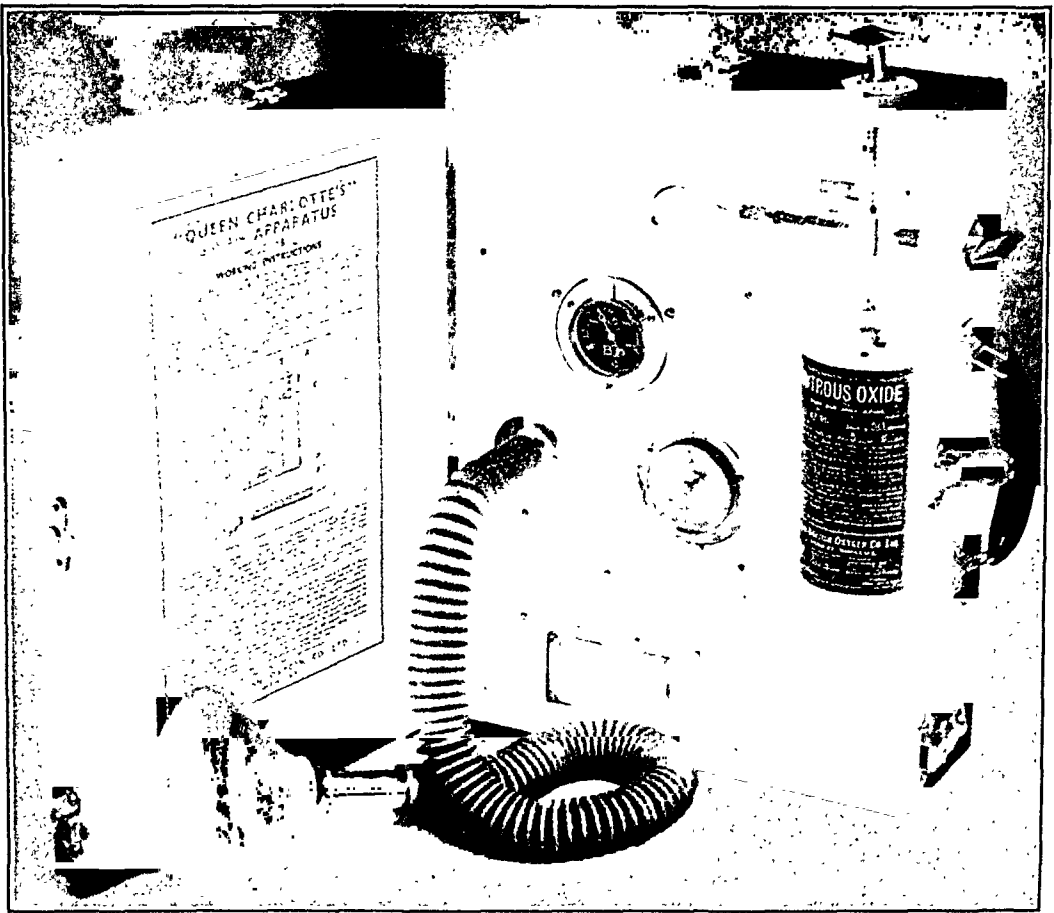


Fig. 1.

breaths of gas and air, patients are quite insensitive to all pain, or at least do not care whether they have pain or not.

There is some little division of opinion as to what is the best percentage of nitrous oxide in air. Dr. Minnitt advises 45 per cent nitrous oxide, but we do not consider this enough, and to all our patients we have administered 60 per cent nitrous oxide in air. We have seen no ill effects whatever resulting from this percentage and patients do not become cyanosed, and we have no difficulty with asphyxiated babies. With percentages over 60 per cent, cyanosis does occur in some cases, although some patients tolerate 70 per cent gas very well.

Gas and air will not suffice for forceps delivery, but we find that we can satisfactorily insert two or three stitches to repair a small tear of the perineum after the patient has had about 20 breaths of gas.

shilling piece. There are two reasons for this. First, *cost*: Nitrous oxide gas in this country costs 5 shillings per 100 gallons, and our average cost has worked out at 2/6 per case, which means that our average period of administration was one hour. In some cases the gas and air was administered for shorter periods, in others, longer.

We find the average consumption of nitrous oxide is about 50 gallons per hour, intermittent flow, and as hospital committees are always closely watching every item of expense, the cost of gas must not be very high.

Our longest case was a twenty-five-hour administration, but however long the administration lasted, no ill effects were observed.

Second, we never have quite so many nurses as we would like, and once the administration of the analgesia has been started, the patient must never be left, and it is not always practicable to keep a nurse constantly beside a patient for several hours.

We do not as a rule give sedative drugs in the early stages of labor, not because we do not believe in their use, but because we feel that after a sedative drug has been administered, the patient must be closely watched, and our staff is limited.

For my own cases in private practice, I always administer some sedative early in labor, and I find that by this means the value of the inhalation analgesia is enhanced. I usually give 1/4 gr. of morphia, but have obtained good results with sodium soneryl.

At the Wellhouse Hospital, I have recently analyzed a series of 1,500 consecutive cases and found that 541 primiparas experienced no pain whatever after the administration of gas and air was started and 331 primiparas obtained great relief, but 8 obtained no relief whatever. There were 332 multiparas who experienced no pain, 280 multiparas had great relief, and 8 were disappointed.

It will be seen then that we have obtained a high degree of success from a method which can be used for all women whatever their situation, and by whomsoever they may be attended.

In most of our municipal hospitals the conduct of a normal confinement is left in the hands of a competent midwife, and it has been shown that the midwife can take complete charge of the administration of the analgesia with conspicuous success.

In the home those who are attended by the general practitioner make use of Dr. Minnitt's method. The gas and air is nearly as much help to the doctor as to the patient. He is no longer called upon by anxious relatives to "do something" because of the patient's distress, and he need not be present during the administration of the analgesia, but can be sent for by the nurse when his presence is required.

Steps are now being taken to arrange that all those patients who are attended by midwives in their own homes, without the presence of a doctor, shall have the advantages which gas and air can give.

It was felt that the principal difficulty in the way of a general adoption of gas and air analgesia was that midwives could not be expected to carry heavy gas cylinders and bulky or expensive apparatus, but two new easily portable machines have recently been produced. The whole apparatus (Fig. 1), gas cylinder, and all fits into a small case and can easily be carried on a midwife's bicycle or in the doctor's car without any inconvenience.

I cannot help feeling that there must be an opening for this gas and air technique in the United States, because there must be many areas where no hospital facilities are readily available, and I believe, as in this country, that the great majority of women are delivered in their own homes.

We do not claim that gas and air gives absolute relief from all pain, but in the great majority of cases, labor is robbed of its terrors.

It has been argued that there is no technique of administration of gas and air, but I regard the technique as extremely important, and I find that the degree of success obtained from gas and air depends on the amount of trouble taken by the attendant. Attention must be paid to small details. Care must be taken to see that the apparatus is in order, that the cylinders contain gas, and that the gas is turned on.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Pathologic Labor

Jungman, Gerhard: *New Viewpoints of the Question of Deflexion Attitudes*, Ztschr. f. Geburtsh. u. Gynäk. 112: 183, 1936.

The author concludes from his study of ten cases in which there were exaggerated deflexions of the head that the condition is entirely due to the shape of the fetal cranium. He believes that deflexion will occur when the cranium is longer than normal in the region of the occiput. The greater size of the occiput compared with the sineiput prevents it from going deep in the pelvis as it necessarily encounters more resistance.

E. S. AUER.

Jacobs, J. Bay: *Persistent Occipito-Posterior—A Simple and Safe Method of Treatment with the Use of a New Forceps*, South. M. J. 29: 891, 1936.

Occipitoposterior presentation is a frequent cause of prolonged labor and dystocia. Present-day widespread use of obstetric analgesia is a definite contributing factor to the causation of this condition, since the patient's cooperation in the use of her voluntary efforts is lacking.

A large percentage of occipitoposterior rotations given enough time will rotate anteriorly spontaneously, but intervention by skilled men considerably shortens labor and yields very good results.

The author presents and describes his obstetric forceps which permit rotation of the posterior occiput and extraction with a single application. In size and appearance they resemble Tucker-McLane forceps.

The stressed advantages of the forceps are: (1) Proper cephalic application of forceps is easily made; (2) necessity for alteration of position of blades or for their reapplication is obviated and thus the head cannot rotate posteriorly; (3) it is the simplest method yet proposed for treatment of occipitoposterior rotation.

ARNOLD GOLDBERGER.

Nandi, Gorachand: *Habitual Breech Presentation*, Calcutta M. J. 31: 289, 1936.

A discussion is presented of the clinical phenomenon of breech presentation occurring repeatedly in the same woman. In the literature Dahlem first drew attention to this condition in 1886 when three cases were reported, two of whom had 5 children, all in breech presentations. Since then numerous cases have been reported with habitual breeches occurring from 3 to 9 times in the same woman.

The etiology is primarily the absence of those factors that lead to a cephalic presentation. Accommodation and gravity are the chief causations of head

There are types of patients who do not benefit from gas and air analgesia. The very nervous patient, the very heavy patient, and the patient who has had previous experience of delivery under full anesthesia are sometimes dissatisfied, but these only constitute a small percentage of the total.

We do not claim by means of gas and air analgesia to give the absolute complete relief that the skilled anesthetist can give with nitrous oxide and oxygen, but we do claim that this method provides a safe and practical means of relieving pain in the second stage of labor for that vast number of women who are unable to engage a skilled anesthetist to attend them in their confinements.

John Elam, M.D.

48 STATION ROAD,
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Frigyesi, J.: The Operative Treatment of Tuberculosis of the Adnexa, Monatschr. f. Geburtsh. u. Gynäk. 105: 193, 1937.

It is now well established that tuberculosis of the female genitalia is secondary to a similar local process elsewhere in the body or to generalized tuberculosis. Frigyesi has observed 22 such cases. In 4 of them Aschheim-Zondek tests were done and in 2 the result was positive. In 5 of the 22 cases a correct diagnosis was made before operation.

The treatment has changed considerably during the last few years. Many authorities are now opposed to operation because of the high mortality and morbidity especially on account of bowel injuries. Roentgen ray therapy is followed by diminution in the size of the masses, and the symptoms subside.

Among the 17 operated patients, 7 were cured, 4 were improved, 3 were unimproved and 3 could not be traced.

The author is of the opinion that operation should be avoided. In cases of doubt a laparotomy is advisable. When conservative and general treatment fail to produce a cure, an operation may be performed with a fairly good prognosis.

J. P. GREENHILL.

v. Pallos, K.: Symptomatology and Pathology of Granulosa Cell Tumors, Monatschr. f. Geburtsh. u. Gynäk. 105: 139, 1937.

According to v. Pallos there have been recorded about 400 cases of granulosa cell tumors in the literature. He reports three cases.

It is almost universally believed at present that these tumors are histologically malignant but clinically benign. In an analysis of about 200 well-described cases, the author found that pain was present in 7.6 per cent, ascites in 8.1 per cent, loss of weight in 4 per cent, inoperability in 0.7 per cent, and recurrences in only 4.5 per cent. The incidence of recurrence in ovarian carcinomas is over 50 per cent.

It is commonly believed that the proper treatment is simple removal of the tumor. On the other hand there is a difference of opinion as to whether or not radiation therapy should be applied. v. Pallos believes that radiation therapy should not be employed because half of these tumors occur in women who are in the reproductive era and because the tumors are clinically benign. However, since we cannot tell which tumors will turn out to be clinically malignant, patients who have had granulosa cell tumors must be watched closely after operation. Bleeding will nearly always indicate a return of the growth.

J. P. GREENHILL.

Rosenfeld, Samuel S.: Podalic Version, Am. J. Surg. 31: 103, 1936.

One hundred twenty babies were delivered by podalic version, employing the Potter technique. There was a real indication for version in every case. The corrected fetal mortality was 3.3 per cent, only slightly higher than in a series of normal deliveries.

Given good obstetric judgement, podalic version is an ideal procedure for the lesser degrees and in some cases even of moderate degrees of pelvic contractions or disproportions. It is also of great value in malposition such as posterior occiput, transverse and face positions. The Potter technique is the preferred method. In cases where difficulty is experienced in the delivery of the aftercoming head, forceps should be applied more often.

J. THORNWELL WITHERSPOON.

Kelly, J. B.: Belated Transverse Presentation with Recovery in Twin Pregnancy, Brit. M. J. 1: 311, 1936.

A case is reported of a twin pregnancy in which one fetus presented transversely and on admission to the maternity hospital had prolapsed a foot, a hand, and a loop of cord. Delivery occurred rapidly. The first born was moribund, but recovered in spite of prolonged pressure on the cord antenatally. The circulation was also restored in the prolapsed foot which had looked almost black before birth. Two placentae were present. A large blood clot was present between the two placentae.

F. L. ADAIR AND S. A. PEARL.

Cordua, R.: Delivery of a Soft Head, Zentralbl. f. Gynäk. 60: 2295, 1936.

Wieland (in 1908) has proved that unusual softness of the baby's skull is not due to rachitic changes but is the result of abnormal processes of apposition and resorption of otherwise normal bone tissue. There is apparently no relationship between this condition and the various disturbances of ossification such as osteogenesis imperfecta, osteopsathyrosis congenita, chondrodystrophia fetalis, etc.

Two cases came under the author's personal observation. In the first case the baby was craniotomized because all other attempts at delivery had failed. Subsequent examination revealed a widened sagittal suture with marked enlargement of both fontanels. On the slightest pressure the soft parts were seen to bulge like vesicles. In the second case the sagittal suture was also widened, both parietal bones and the occipital bone were thin and soft and there was also a spina bifida. Following an operation for the latter condition, the child died on the fourth day after delivery.

The author states that in these cases it is very difficult, if not impossible, to diagnose correctly the presentation because of the alterations of the fontanels. These heads, furthermore, are delivered spontaneously, only with great difficulty owing to the elasticity of the presenting part. Application of forceps usually leads to severe injury of the head.

RICHARD SOMMA.

Marx, A. N.: A Remarkable Case of Precipitate Labor, Med. Klin. 32: 734, 1936.

A correct diagnosis of precipitate labor has an important bearing on forensic medicine. It is not possible to make a definite diagnosis of precipitate labor from an examination of mother and child alone. It is always best for the judge to instruct the mother to give a detailed account of the labor in her own words. In all cases of precipitate labor both mother and child run a number of risks. If the cord tears during the fall of the baby the latter may bleed to death or suffer

presentation. In the majority of cases of breech an habitual condition is present. Pelvic contractions, abnormality of size and shape of the head, pathologic anomalies of the head, abnormalities in the shape of the uterus, prematurity, and hydramnios are all predisposing causes. Multiparity, twins, and fetal macerations are frequently associated with breech presentation. The hereditary and individual tendency must be recognized.

F. L. ADAIR AND S. A. PEARL.

Goethals, Thomas R.: *The Risk to the Infant in Breech Delivery*, Surg. Gynec. Obst. 62: 525, 1936.

In the 1,242 breech deliveries in the Boston Lying-In Hospital during the years from 1913 to 1934, the gross combined fetal (stillbirth) and neonatal death rate was 25.7 per cent. In 272 deliveries, either the pregnancy was pathologic, with such complications as preeclamptic toxemia, eclampsia, nephritis, syphilis, diabetes, hydramnios, etc., or labor was complicated by such conditions as placenta previa, ablatio placentae, or prolapse of the cord, with a crude mortality rate of 51.8 per cent; and resulted in the birth of 43.3 per cent of premature infants, with a crude mortality rate of 82.2 per cent.

In the 970 deliveries uncomplicated by pathologic pregnancy, the crude mortality rate was 18.5 per cent; uncomplicated deliveries produced premature infants in 15.7 per cent of the cases, with a crude mortality rate of 62.1 per cent.

Placenta previa, ablatio placentae, and prolapse of the cord are respectively three, five, and five times more often associated with breech presentation than are all types of delivery.

The mortality rate was 13.6 per cent among 916 newborn infants (excluding macerated and grossly malformed babies), subdivided as follows: 53.6 per cent for premature, 10 per cent for immature, and 6.9 per cent for mature infants. This last figure represents the risk to the living, undeformed, full-term infant in utero who is destined to be born by breech delivery in the absence of pathologic pregnancy and of hemorrhage and other accidents of labor due to abnormalities of the placenta or of the umbilical cord.

WM. C. HENSKE.

Soule, S. D.: *Breech Delivery*, J. Missouri M. A. 33: 449, 1936.

A series of 328 breech deliveries is reported with a combined ward-private service fetal mortality of 7.45 per cent. Traumatization is the chief cause of mortality in breech delivery. Prolonged second stage of labor, cervical dystocia and difficulty with the aftercoming head account for most of this traumatization. A "hands-off" policy is to be observed until dilatation of the cervix is complete. Spontaneous delivery of the breech is preferred if progress is steady. With a delay of longer than two hours in the second stage of labor the breech is pushed up, decomposed, and extracted. Complete breeches and footlings are delivered as soon as dilatation of the cervix is complete. Episiotomy is performed as soon as the vulva is distended. Traction on the aftercoming head is to be eliminated so far as possible. The Wigand-Martin maneuver is preferred to all other manual procedures for delivery of the aftercoming head, the abdominal hand serving to aid flexion only. If any resistance is encountered, Piper forceps are applied to the aftercoming head. The increased fetal mortality in multiparae in this series is definitely associated with fetal weight of more than 3200 gm. Breech delivery is an obstetric complication of major consequence.

J. THORNWELL WITHERSPOON.

describes the customary treatment of obstetric hemorrhages. Measures to combat shock should take time-precedence over measures to control bleeding.

In respect to the cause of postpartum hemorrhage, routine examination of cervix and deep vagina for lacerations should be a first consideration, particularly after instrumentation. Secondary uterine atony, the next most common cause, is attributable largely to mismanagement of the third stage through neglect to observe the progress of events within the uterus and also to a desire to hasten its termination. Pure inertia uteri should be treated by pressing the lower uterine segment against the sacrum and by compression of the corpus between one hand on the abdomen and the other in the vagina. Oxytocics may be repeatedly applied. The author does not advocate packing of the uterus because it is unphysiologic and carries the risk of infection.

ARNOLD GOLDBERGER.

Carcoux: Uterine Ruptures Observed in the Hanoi Maternity from 1930 to 1934, *Gynéc. et d'obst.* 33: 366, 1936.

Carcoux reviewed a series of 52 cases of uterine rupture. Not one of the patients was a primipara and only one was a secundipara. All the other patients had had from 3 to 13 children. The 3 important symptoms of this complication were hemorrhage, shock, and infection. In all of the cases the fetus was expelled into the abdominal cavity and in all the cases the placenta had separated at the time of operation. The most important factor in the death of women who died quickly was shock. In all but 2 cases the condition was treated by subtotal hysterectomy. There were 23 deaths in this series, most of them due to generalized infection or peritonitis. Two women died of secondary hemorrhage. Some authorities maintain that if the fetus is not entirely free in the abdominal cavity it should be extracted from below. The author, however, warns that this is a very dangerous procedure.

J. P. GREENHILL.

Vitamins and Pregnancy

Gaechtgens, G.: The Daily Need of Vitamin C in Pregnancy, *Arch. f. Gynäk.* 164: 571, 1937.

The author carried out prolonged studies on the vitamin C needs of ten healthy pregnant women. Using the Widenbauer method, he determined the daily need of cevitamic acid to be 33 to 64 mg. Thus the daily requirement of vitamin C is not greater for the pregnant than for the nonpregnant woman. The usual deficiency found during pregnancy is probably due to the needs of the fetus and the passage of the vitamin C through the placenta. The addition of 100 mg. of vitamin C to the daily diet of the pregnant woman will prevent the appearance of any vitamin C deficiency.

RALPH A. REIS.

Gaechtgens and Werner: Vitamin C Deficiency During Pregnancy and Lactation, *Klin. Wchnschr.* 16: 843, 1937.

The authors used the Jeszler-Kapp method for determining the vitamin C content during pregnancy and lactation. A marked deficiency of vitamin C was found in 62 per cent of the primiparas and in 70 per cent of the multiparas examined. In those women in whom a vitamin C deficiency was ascertained, tests showed the same general deficiency during the lactation period. Apparently no compensatory rise occurs.

RALPH A. REIS.

severe cranial and intracranial injury. The child may suffocate if measures are not taken to see that it breathes properly. Precipitate labors frequently result in expulsion of a baby into a toilet. This is usually brought about by the fact that patients in labor experience a desire of having a bowel movement. The author reports a very interesting case which had marked legal significance. In this case the child was expelled into the toilet by the patient without her knowledge. The child was subsequently found alive. The author points out many pitfalls which would have led some jurists to the erroneous impression that the mother had purposely thrown the child into the toilet.

J. P. GREENHILL.

Trillat, E.: *Statistics of Postpartum Hemorrhage in 10,000 Deliveries*, Bull. Soc. d'obst. et de gynec. 25: 247, 1936.

The author's criterion of postpartum hemorrhage is a loss of 500 c.c. or more of blood. In a series of 10,000 labors he found that 703 patients lost more than this amount, an incidence of 7 per cent. Twenty-three patients lost between 1,500 and 2,000 c.c., and 5 patients between 2,000 and 2,500 c.c. of blood. The uterus was invaded in 104 of the 703 cases. There were 10 deaths in this series representing an incidence of 1.4 per cent. Strange to say, there were no deaths among the 5 women who lost more than 2,000 c.c. of blood. There were 7 deaths among 557 women who lost between 500 and 1,000 c.c. of blood, one death among 108 women who lost between 1,000 and 1,500 c.c. of blood, and 2 deaths among 23 women who lost between 1,500 and 2,000 c.c. All the patients who died had evidences of infection.

J. P. GREENHILL.

Herold: *The Treatment of Postpartum Hemorrhage With Special Consideration of the Henkel Treatment*, Monatschr. f. Geburtsh. u. Gynäk. 103: 1, 1936.

In reviewing the literature on the use of the Henkel method of stopping hemorrhage in cases of profuse postpartum bleeding, the author found reports of 200 cases. He also obtained information concerning about 300 additional cases, and with the exception of one case of a vesicovaginal fistula which Henkel himself described, no harm has resulted following the use of the Henkel procedure. The author therefore recommends the method which consists in the temporary application of a clamp through the vagina to the uterine artery on each side of the cervix. He recommends this procedure in cases of cervical lacerations, uterine atony and also of placenta previa, and premature separation of the placenta.

J. P. GREENHILL.

Cosgrove, S. A.: *Obstetric Hemorrhage and Its Management*, South. M. J. 29: 1219, 1936.

Of the lethal triad, sepsis, hemorrhage, and toxemia, hemorrhage accounted for the highest number of purely obstetric causes of death in the author's experience.

Because of the seriousness of this complication it is vital to anticipate it.

The frequent association of bleeding with the toxemic states stresses the importance of careful prenatal supervision. Gravid patients must be instructed concerning the significance of bleeding and the importance of prompt report of its occurrence. Routine blood grouping of antenatal patients is desirable. Hospitals must be ready for rapid and efficient treatment of hemorrhage. The author

ulcerative colitis from which the patient was suffering during her pregnancy. This deficiency was corrected by parenteral administration of vitamin. The author discusses the entire problem of avitaminosis and calls attention to the especial danger of this condition arising during pregnancy when there is any co-existent gastrointestinal disease present. In the presence of such a combination the deficiency must always be corrected.

RALPH A. REIS.

Chatterjee, Sachindra Nath: Role of Diet During Pregnancy With Special Reference to Vitamins, *Indian Med. Rec.* 55: 200, 1935.

The diet of the expectant mother should consist of simple nutritious foods, mixed in character, containing fruits, vegetables, rich in mineral and vitamins, as well as milk from healthy cows. The urine should be checked regularly and if albumin is present, the protein foods, eggs, fish, meat and, if need be, milk should be restricted. A well-balanced diet will provide the necessary calcium and phosphorus for mother and fetus. Foods rich in iron and copper must be provided, i.e., spinach, liver, apples, etc. Vitamins are very important in the diet of the pregnant woman. All the vitamins from A to E should be administered. They play a great part in the development of immunity and, therefore, lower morbidity and mortality in mother and infant.

F. L. ADAIR AND S. A. PEARL.

Watson, E. M.: Clinical Experiences With Wheat Germ Oil (Vitamin E), *Canad. M. A. J.* 34: 134, 1936.

Watson prescribed wheat germ oil to 65 patients in whom spontaneous abortions, threatened abortions or involuntary sterility constituted the principal abnormalities.

In the majority of the abortion and sterility cases no therapeutic measures except the use of wheat germ oil were instituted. But the patients with signs of threatened abortion furthermore were subjected to the management usual for that condition. Of eleven patients who previously had from 3 to 15 spontaneous abortions, 9 went to term and were delivered of healthy living children. Six of the patients under this regimen completed a pregnancy for the first time. Of the 17 wheat germ oil treated patients, each of whom had had 2 spontaneous abortions, 12 gave birth to healthy living children after the use of the oil. In 5 cases the pregnancies were interrupted by spontaneously occurring abortions. Of 9 treated patients, each of whom had experienced one previous spontaneous abortion, 8 gave birth to healthy, living children. In the ninth, one abortion took place a short time after the use of the oil was commenced. Fifteen patients were treated for the symptoms of threatened abortion, the majority after bleeding had begun. In 11 of these the pregnancies continued uninterruptedly to term, but in 4 the abortion became inevitable. Thirteen nonpregnant women were given wheat germ oil with a view to facilitating impregnation. Six of these had never conceived and therefore constituted examples of primary sterility. Each of the remainder had been pregnant at least once. Seven had had one or more abortions, but only one woman had given birth to a living child. Pregnancy did not ensue in any of the patients in this group. The experiments lend some support to the surmise that vitamin E is a factor in the advancement of pregnancy to a natural termination.

J. P. GREENHILL.

Theobald, G. W.: Effect of Calcium and Vitamins A and D on Incidence of Pregnancy Toxemia, *Lancet* 1: 1397, 1937.

This study centered about the possible influence of additional calcium and vitamins A and D on the incidence of toxemia of pregnancy. A series of 100 patients, not more than twenty-four weeks pregnant, were divided into two units of 50, one for the control. The members of the other group were requested to take daily 20 gr. of calcium lactate, 11,000 (international) units vitamin A, and 450 units of vitamin D.

Gaetgens, G.: The Passage of Carotin and Vitamin A From the Maternal to the Fetal Circulation, Arch. f. Gynäk. 164: 398, 1937.

Comparisons were made of the amount of carotin and vitamin A in the venous blood of 23 women during labor and the content of umbilical cord blood. Vitamin A was never found except in traces and carotin in only very small quantities in the fetal circulation. No definite relation could be ascertained between the quantities in the maternal blood (which always contained larger amounts) and in the fetal blood. The passage of vitamin A and carotin from the maternal circulation to the fetal circulation cannot be entirely explained on simple physicochemical changes. There must be some other regulatory mechanism which permits only certain small amounts to pass through the placenta, first, to prevent a hypervitaminosis of the fetus and, second, to prepare the fetal liver for its post-partum function of storing vitamin A and carotin.

RALPH A. REIS.

Neuweiler, W.: Vitamin C and Placenta, Arch. f. Gynäk. 162: 384, 1936.

The author was able to demonstrate the presence of vitamin C in the placenta by indophenol titration, by methylene blue, by the ferment method and by animal experimentation. The concentration of vitamin C depends on the method of extraction. The method recommended by Fujita was found to be inaccurate. The tests during early pregnancy gave findings higher than normal, but the author doubts the reliability of such findings. The vitamin C content is somewhat higher on the maternal than on the fetal side of the placenta. The origin of both is the available vitamin C in the maternal blood stream. The vitamin C is apparently stored in the outer layer of the chorionic villi, thus assuring a continuous supply for the fetus.

RALPH A. REIS.

Tonutti and Plate: Vitamin C in the Human Placenta, Arch. f. Gynäk. 164: 385, 1937.

The authors were able to demonstrate the presence of vitamin C in the human placenta, in the decidua, the syncytial, and in the stroma cells. The decidua maintains a constant level of concentration in the placenta, since the vitamin C passes rapidly through both the syncytium and stroma. An increase in vitamin C intake is immediately evidenced by an increase of the substance in the placenta. In all patients studied there was found a vitamin C deficiency. (This investigation was carried out entirely during the winter months.)

RALPH A. REIS.

Bentivoglio, Franco: Maternal-Fetal Metabolism of Vitamine C, Folia Gynaec. (Genova) 33: 207, 1936.

The author made quantitative determinations of the amount of ascorbutic acid (vitamin C) in the blood and organs of guinea pigs in various states of gestation and under varying dietary regimes.

The most notable finding was that accumulation of vitamin C in various organs during pregnancy was much less than in the nongravid state. The author believes that there is no overproduction of vitamin C during pregnancy but that there is a liberation of this vitamin into the blood from deposits in the organs.

When the animal is kept on a vitamin free diet the vitamin values are higher in the fetus than in the mother. The author feels that the possibility cannot be excluded that a slight amount of synthesis of vitamin C occurs in the fetus.

MARIO A. CASTALLO.

Gaetgens, G.: Avitaminosis of Pregnancy as the Result of Intestinal Disease, Klin. Wehnschr. 16: 445, 1937.

The author reports a case of marked avitaminosis during pregnancy. There was a marked deficiency of vitamin C which the author believes to have been due to an

Items

American Board of Obstetrics and Gynecology

The oral, clinical, and pathological examinations for Group A and Group B applicants will be held in San Francisco, California, on Monday and Tuesday, June 13 and 14, 1938.

An informal dinner for the Diplomates of this Board, their wives and others interested in the work of the Board, will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, will address the group, and the successful candidates of the preceding two days' examinations will be introduced in person. Tickets, at \$2.25 each, may be obtained in advance from Dr. Joseph L. Baer, 104 S. Michigan Avenue, Chicago, Illinois, or at the door. Reservations should be made in advance if possible.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

American Committee on Maternal Welfare

A meeting of members and directors is called for Thursday, June 16, 1938, at 6:30 P.M., at the Palace Hotel, San Francisco, Calif., for the purpose of electing directors and for the transaction of other business which may be presented.

Also there will be an open luncheon meeting of the Committee on Maternal Welfare, on Wednesday, June 15, 1938, at 12 noon, in the Borgia Room, St. Francis Hotel. This is to be followed by a business meeting at which will be discussed the program of the forthcoming American Congress on Obstetrics and Gynecology to be held in Cleveland, Ohio, September 11 to 15, 1939.

All those interested are invited to attend. For further information address the Headquarters office, 650 Rush Street, Chicago, Ill.

In the group on regular diet, 28 patients showed evidence of toxemia, while only 13 of those taking calcium and vitamins A and D had such symptoms.

These results strongly suggest that a main factor in the prevention of toxemia is the vitamin-B complex. The author recommends that others make similar observations. The writer asserts that the difference between the two groups in this series is too great to be explained by chance.

H. CLOSE HESSELTINE.

Shute, E.: Anti-Proteolytic Properties of Human Blood Serum in Cases of Miscarriage and Premature Labour, J. Obst. & Gynaec. Brit. Emp. 44: 253, 1937.

The literature dealing with the vitamin deficiencies and the hormonal factors concerned with premature interruption of pregnancy in animals and man is discussed by Shute. A large percentage of patients who miscarry or are prematurely delivered show an excess of estrogenic substance in the blood serum. This produces a resistance in that blood serum to its digestion by such a proteolytic enzyme as trypsin. This resistance to proteolysis temporarily disappears from the maternal blood on administration of an adequate quantity of fresh vitamin E and simultaneously symptoms and signs of impending labor cease. With cessation of vitamin E therapy, this estrogenic substance usually reappears in the blood, and coincidentally symptoms and signs of threatened labor may show themselves again.

J. P. GREENHILL.

Vogt-Moeller: Treatment of Habitual Abortion With Wheat Germ Oil (Vitamin E), Klin. Wehnschr. 15: 1883, 1936.

Vogt-Moeller reports results obtained in his last 56 cases of habitual abortion. To obtain living children he prescribed vitamin E in the form of wheat germ oil. He was rewarded by delivery of 38 full-term babies.

J. P. GREENHILL.

Dicker, S.: Treatment of Vomiting of Pregnancy by Ascorbic Acid (Vitamin C), Schweiz. med. Wehnschr. 67: 74, 1937.

Eight cases of severe hyperemesis gravidarum were treated with vitamin C by Dicker. In all the cases there was a sudden cessation of symptoms or at least a decided and progressive improvement. The author administered vitamin C by the intravenous route. The favorable action is due to restoration of the thyroid-vitamin C equilibrium.

J. P. GREENHILL.

Brehm: Potential Dangers of Viosterol During Pregnancy: With Observations of Calcification of Placenta, Ohio State M. J. 33: 990, 1937.

Some obstetric patients need more calcium and vitamins than provided by a normal diet. In the opinion of Brehm viosterol causes definite calcification in the placenta, which is greatly increased by the ingestion of calcium. Viosterol may also be responsible for calcification in the kidney of the newborn. Cod liver oil seems preferable to viosterol or irradiated ergosterol. Natural vitamins, when indicated, seem preferable to synthetic products. It is important in treating a patient not to produce by overtreatment a more serious condition than the one originally treated. Considerably more research is required before the promiscuous use of viosterol during pregnancy can be continued.

J. P. GREENHILL.

and especially of the biologic properties of these neoplasms. For the group differs from other ovarian cancers in that some of its members are made up of cells which retain a functional capacity manifested often by profound effects upon the sex characters of the patient. This general subject has been discussed in a previous paper by us,¹ so that here only a short summary is necessary as a background for the discussion of one member of this group of tumors; viz., the disgerminoma.

In its earliest stages the anlage of the gonad is a collection of cells on the anterior or ventral surface of the Wolffian body, cells which in this undifferentiated phase of gonadal development possess neither male nor female attributes, for the spark of sex has not yet been applied. Just what this spark is cannot be stated with certainty, though many biologists believe that in the human being, as in some of the lower animals, it is the entrance of the germ cells into the gonadal area after migration from a much earlier situs. Once this

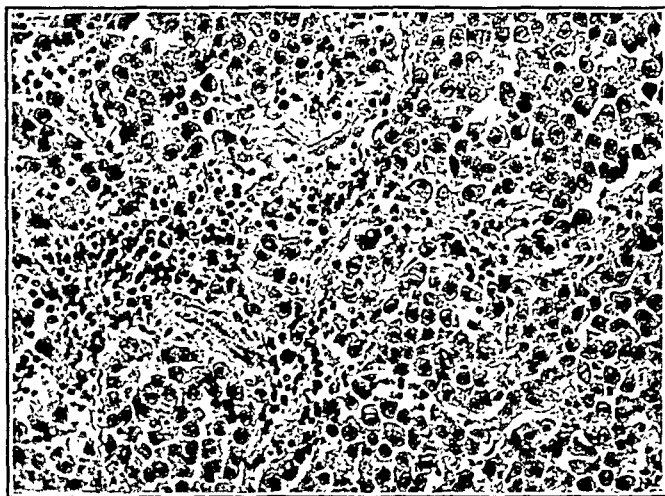


Fig. 1.—Typical seminoma of testis, identical histologically with disgerminoma of the ovary.

spark has been applied, the sex direction of gonadal development is determined along ovarian or testicular lines, as the case may be. Tumors arising from gonadogenic elements in this differentiated phase of the sex gland area may develop in later life, producing the feminizing granulosa cell carcinoma or the masculinizing arrhenoblastoma, as has been discussed in previous papers (Novak and Long,² Novak and Brawner³).

In this communication, however, we are concerned with tumors which may arise from cells which date back to the undifferentiated stage of gonadal development, before its cells have become tintured with either female or male attributes. Such an origin, first suggested by Robert Meyer,⁴ has been ascribed to the so-called seminoma of the ovary. It receives much support from the fact that an exactly identical tumor is found in the testis (Fig. 1), as would be expected if the origin is from cells which stray away from the germinal stream in gonads which may later develop into either testes or ovaries. The

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Original Communications

DISGERMINOMA OF THE OVARY

CLINICAL AND PATHOLOGIC STUDY OF 17 CASES

EMIL NOVAK, M.D., AND LAMAN A. GRAY, M.D., BALTIMORE, MD.

(From the Department of Gynecology, Johns Hopkins Medical School)

NEXT to the uterus, the ovary is the most frequent site of malignancy in the female generative organs. Ovarian carcinoma in general is of a high degree of malignancy, the five-year curability rate being commonly put at between 10 and 15 per cent (Lynch, Healey). There are certain forms of ovarian cancer, however, which are much less unfavorable than others, and it is of obvious importance to both the clinical gynecologist and the pathologist to be able to sift these out from the material which comes under observation. Taken as a group there is no doubt that the four malignant ovarian tumor types which have come to be spoken of as "special ovarian tumors" offer a far more favorable prognosis than does ovarian cancer in general. To this group belong granulosa cell carcinoma, arrhenoblastoma, disgerminoma, and the so-called Brenner tumor. The last named of these, as a matter of fact, is of so low a degree of malignancy that it may very well be classed as an essentially benign tumor.

The other three tumor types are unquestionably to be classed as malignant on both clinical and histologic grounds. Our knowledge of their histogenesis is not by any means complete, but even so we know more on this point than we know concerning most other ovarian cancers. While our views as to the histogenesis of this group are in some respects conjectural, the satisfactory working theory now generally accepted fits in quite well with our knowledge of the pathologic

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

For, example, one of Fauvet's⁷ patients was 52 years old. The age distribution in our own series of 17 cases may be considered to be fairly representative. It was as follows: 6, 10, 12, 15, 16, 16, 18, 18, 19, 20, 22, 22, 22, 23, 31, 36, 38. Our youngest patient, therefore, was 6, and the oldest, 38, with an average of about 20. Thirteen of our patients were white, and 4 were colored.

Gross Pathology.—The size of disgerminomas varies between wide limits, some measuring only a few centimeters in diameter, others being so large as to fill the abdominal cavity (Case 13) (Fig. 2). Characteristically they are surrounded by a smooth, rather dense capsule, though the contour may be slightly nodular (Fig. 3). The consistency of the tumor, which is essentially a solid one, has often been described as "doughy," but a better adjective would often be "rub-

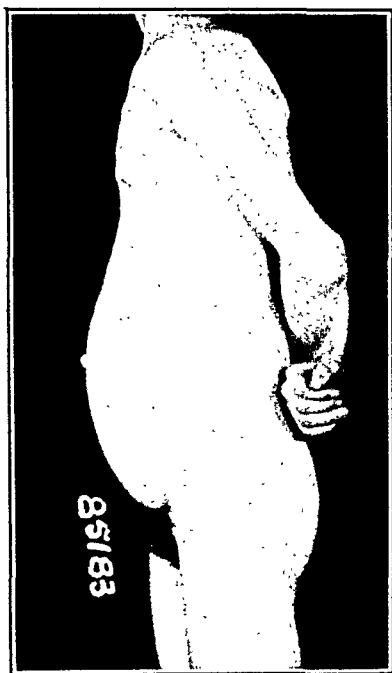


Fig. 2.

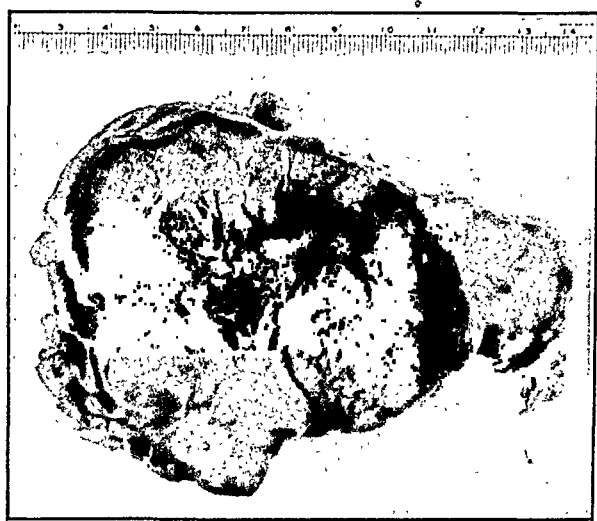


Fig. 3.

Fig. 2.—Side view of patient in Case 13 (kindness of Dr. R. H. Jackson, Madison, Wis.). The patient was 10 years old and the tumor weighed nearly 5 pounds. It was of very malignant type, with death three months after operation.

Fig. 3.—Gross appearance of infiltrating disgerminoma in Case 8. The patient, aged 8, received postoperative radiation, and is living four years after operation (see Fig. 6).

bery." The cut surface is grayish or grayish-pink, with almost always areas of distinctly yellowish hue. Areas of necrosis, degeneration and hemorrhage are quite characteristic, though there is little tendency to the formation of cysts, as with granulosa cell carcinoma. The tumors are generally unilateral, but may involve both sides (Kleine,⁸ our Case 3). Ascites is often observed, as with other solid ovarian growths. In at least one previously reported case torsion of the pedicle has been observed (Kleine), and a similar occurrence was noted in one of our cases (Case 11). In 2 of our cases there was an associated teratoma of the ovary (Fig. 4).

testicular tumor referred to is the common disgerminoma, called by some embryonal carcinoma. As a matter of fact, the same name was applied by Chevassu⁵ to the ovarian prototype, and is still the popular one in the French literature, though Meyer's designation, disgerminoma, seems more expressive and has been widely adopted.

Another circumstance which suggests the probable correctness of the above theory of histogenesis is the frequent occurrence of such tumors in individuals with subnormal gonadal development or in pseudohermaphrodites. It cannot be too strongly emphasized, however, that in such cases the tumor has nothing to do with the development of the sex anomaly, which will persist even after removal of the tumor. A female pseudohermaphrodite in whose ovary a disgerminoma develops will be just as pseudohermaphroditic after removal of the tumor as before. This is what one would expect in view of the asexual nature of the constituent cells.

In this respect the ovarian disgerminoma differs very sharply from the granulosa cell carcinoma and the arrhenoblastoma. The latter, for example, occurs in individuals with previously normal sex development, who later show marked sex differentiation phenomena (amenorrhea, atrophy of breasts, male body, contour, male hirsutism, enlargement of the clitoris, deepening of the voice) because of the production of the male sex hormone by the tumor cells, since the tumor arises from undifferentiated cells of potentially male type which have persisted in the ovary. In such cases removal of the ovarian tumor is followed by regression of the masculinizing phenomena.

It is because we feel that many gynecologists and pathologists have not yet familiarized themselves with the characteristics of ovarian disgerminoma that we are impelled to a discussion of the subject, especially as we have had the opportunity of studying a considerable group of cases in our laboratory. In past years these tumors were variously diagnosed as carcinoma (the gross-zelliges Karzinom of the Germans), alveolar sarcoma, and even endothelioma. They are considerably less frequent than granulosa cell carcinoma, but more common than arrhenoblastoma or Brenner tumors. In our own material we have encountered 17 disgerminomas, as against 58 granulosa cell carcinomas, 7 arrhenoblastomas and 8 Brenner tumors. Granulosa cell tumors are relatively frequent, our own experience agreeing with that of Klaften,⁶ who finds that they make up about 10 per cent of all primary malignant ovarian tumors and that disgerminoma is a little less than one-third as frequent as granulosa cell carcinoma. Klaften reports 6 disgerminomas to 19 granulosa cell cancers, and, in our own larger series of cases, this proportion seems to hold. Our material comprises 17 disgerminomas and 58 granulosa cell carcinomas, so that in our experience the latter have been about 3.5 times as frequent as the former.

Age.—Disgerminoma is preeminently a tumor of early life, thus justifying the appellation of "carcinoma puellarum." It is common in children before puberty, and likewise in young adolescents. It should be remembered, however, that it is not rarely found in adult women.

Even in small tumors areas of degeneration are seen, and in the larger growths they are both constant and extensive. The same statement may be made concerning hemorrhage. In the degenerated areas especially, one may occasionally find symplasmic giant cell formation, so that in a considerable group of reported cases, the coexistence of tuberculosis has been suspected.

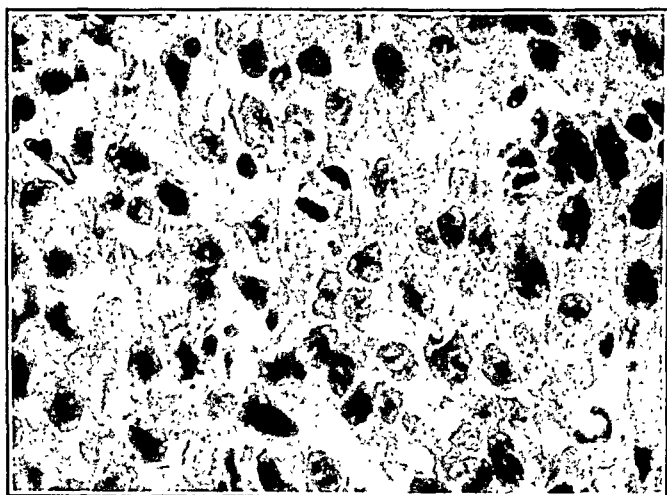


Fig. 6.—High power of tumor in Case 8, showing several mitoses. Patient, aged 6, living four years after incomplete operation followed by radiation (see Fig. 3).

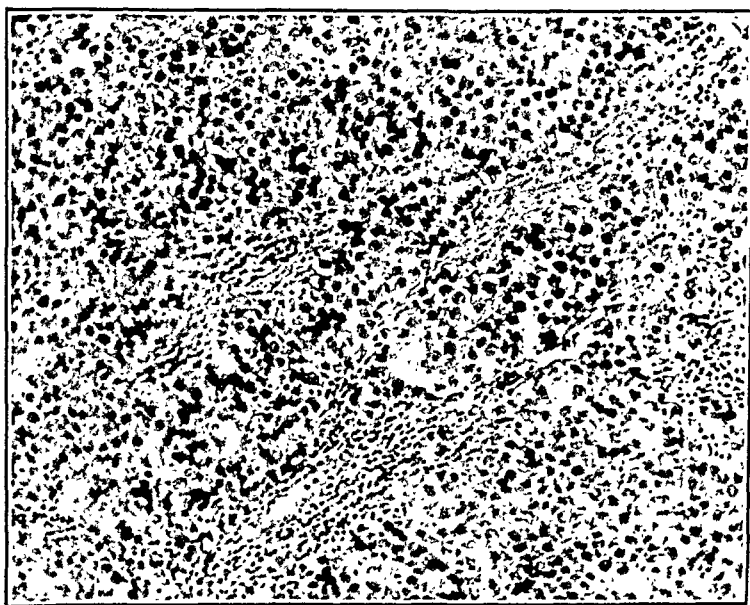


Fig. 7.—Disgerminoma from Case 9 (kindness of Dr. N. P. Sears, Syracuse, N. Y.), patient aged 12. No recurrence after two years. Note typical lymphocytic infiltration of septa.

In one of our cases (Case 12), a considerable number of large giant cells were found in some areas of the tumor, so that there was at least a superficial resemblance to tuberculosis (Fig. 8). As a matter of fact, Kermanner,⁹ in 1925, reported a case in which, as he thought, tuberculosis was associated with a tumor which he himself called granulosa cell carcinoma. Later the same author reported 5

Microscopic.—There are few tumors of the ovary which present such distinctive histologic characteristics as does disgerminoma. This applies to both the cell type and the general architecture of the tumor. For this reason the microscopic recognition is usually very easy, once one has familiarized oneself with the microscopic criteria. There is far more variation in the histology of granulosa cell carcinoma or of arrhenoblastoma, both of which include many possible histologic types. The large round, ovoid or polygonal cells of disgerminoma are responsible for the former designation of this tumor as the "large-cell carcinoma" (grosszelliges Karzinom) (Fig. 5). The cytoplasm is abundant, clear, very pale-staining and often translucent. The nucleus likewise is large, round and stains heavily with hematoxylin. Mitotic figures are seen in varying number, though not usually numerous (Fig. 6).

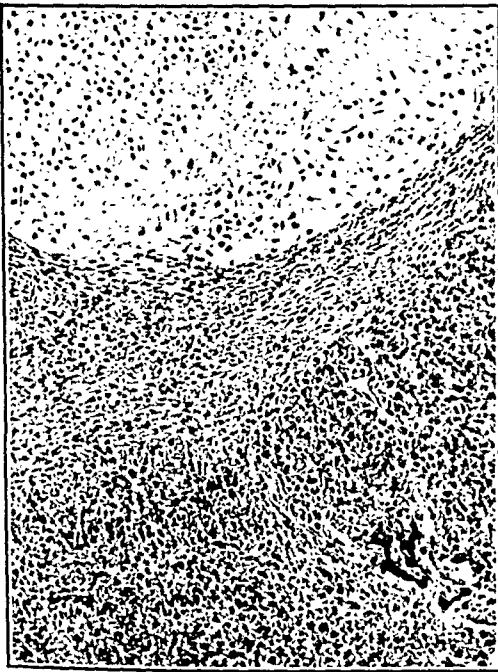


Fig. 4.



Fig. 5.

Fig. 4.—Disgerminoma, combined with teratoma, in Case 12. Note the large area of cartilage above, other parts of the tumor showing typical disgerminoma.

Fig. 5.—Microscopic picture in Case 10 (kindness of Dr. H. N. Allen, St. Louis, Mo.). Note the alveolar arrangement of the tumor cells, with trabeculae of hyalinized connective tissue. Patient aged 38.

Just as characteristic is the arrangement of the cells in alveoli or nests, separated by septa of fibrous tissue which shows more or less hyalinization, and which quite constantly shows extensive lymphocytic infiltration (Fig. 7). Often, especially toward the periphery of the tumor, the cells are arranged in long columns or strands. In some tumors the septa are abundant and thick, while the cell nests are relatively sparse. Others are characterized by marked cellularity with very little connective tissue, and these features are thought by some (Fauvet) to be indicative of a much higher degree of malignancy than in the former group, though we have not been able to confirm this observation.

Malignancy.—As to the malignancy of dysgerminoma in general, there can be no question, though there is much variation in individual cases. Taken as a group they are less malignant than the granulosa cell cancers, but more malignant than the arrhenoblastomas. The number of properly studied and adequately followed cases is as yet too small to make worth while any discussion of proportion of cures or recurrences. However, in 53 adequately reported cases, Doederlein¹¹ found that 13, or about 25 per cent, had extrapelvic metastases, and that 10 of these (18.8 per cent) had died.

From a clinical standpoint three general groups of cases may be described: (1) Those in which the tumor capsule is intact, with no extension beyond the ovary; (2) those in which there is infiltration, at times massive, of other pelvic viscera, such as the uterine ligaments, tubes, bladder, or the pelvic peritoneum; (3) those in which extensive metastasis is seen, usually to the omentum, parietal peritoneum, lymph glands, liver, or other organs.

The first of these groups, especially those in which the tumor is of small size, naturally offers much the most favorable prognosis. It is in this group that unilateral operations have often been successful in curing the patient, though the hazard of recurrence is not by any means eliminated. For this reason, and also because of the usual sterility of the patients, there can be no harsh criticism of those who advocate radical operation in all cases. Even in the second group, with perhaps extensive infiltration and with necessarily incomplete operation, apparent cures have been noted. In patients of this group, the uterus, broad ligaments, tubes and retroperitoneal structures may show extreme involvement.

Recently Schiller¹² has urged the view that the extraovarian involvement in such cases does not represent malignant extension or metastasis, but that it is due to simultaneous neoplastic growth in anlagen of indifferent gonadal tissue at various points along the Müllerian duct, just as ovarian dysgerminoma develops from such an anlage in the sex gland area. In support of this he describes a case of uterine tumor which on morphologic grounds he interprets as a uterine dysgerminoma, occurring in the absence of ovarian dysgerminoma. His evidence, however, seems to us very unconvincing, and the frequent report of cases of dysgerminoma associated with widespread dissemination to organs and tissues not in any way related to the Müllerian canal makes it seem far more likely that the routes of dissemination of dysgerminoma are those pertaining to malignant growths in general. In the third group of cases, for example, the omentum, the parietal wall, the intestine, and other viscera may show extensive involvement, much as is seen in other types of ovarian cancer.

Of our own 17 cases, there were 10 which clinically corresponded to the first of the types above described, and, with the exception of one patient who died of postoperative intestinal obstruction, all these

other somewhat similar cases. Schiller¹⁰ in a subsequent examination of these tumors found them to be disgerminomas. Kermauner's assumption of the presence of tuberculosis in these cases was based on superficial histologic grounds, and in the light of other cases since observed, was quite certainly incorrect. Schiller himself reports two other cases of disgerminoma with giant cells, and in both of these was able to make careful studies, including tissue stains for tubercle bacilli, with negative results.

In one of Schiller's cases (Case 7), the resemblance to a tuberculous process was especially striking, with not only giant cells, but also numerous lymphocytes and epithelioid cells, and in some areas a typical tubercle formation. In this case very thorough studies were made of the patient's general and pulmonary condition, including x-ray examinations, tuberculin tests, and animal inoculations, all with negative results. Tissue stains were likewise negative. On the basis of recent laboratory investigations of tuberculosis, suggesting that

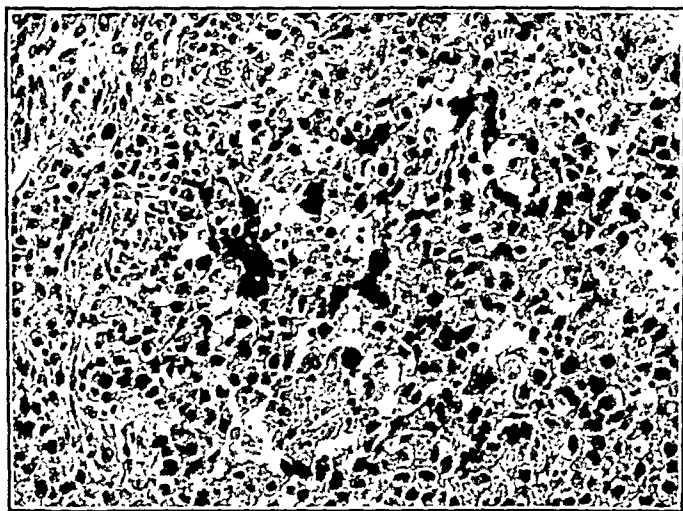


Fig. 8.—Giant cells (symplesmic) in Case 12 (kindness of Dr. B. F. Eckles, Galax, Va.). Patient aged 19.

the characteristic tissue reaction is probably produced by fatty substances of fluid nature, Schiller believes that similar fatty principles may result from the degeneration of the disgerminoma cells, setting up a process almost identical with that of tuberculosis. In addition to the cases already mentioned, Schiller has collected from the literature a number of others (Zimmermann, Atzerodt, Polano-Daube, Von Szathmary), all apparently disgerminomas in which similar pseudo-tuberculous areas were encountered.

In our own case, in spite of the presence of numerous giant cells, the resemblance to tuberculosis is not great, and there would seem to be little doubt that the giant cells are evidences of the degenerative changes which characterize all disgerminomas, with the merging of cells and consequent formation of large polynuclear cell masses, just as is seen in degenerating areas of many other tumors. As a matter of fact, one finds such giant cells only in obviously degenerating areas of the tumor.

followed by radiotherapy, is living and in good general health four years after operation, though a small pelvic nodule is still palpable on rectal examination. The remaining 2 patients have not been traceable.

Associated Developmental and Sex Changes.—In all the earlier papers on disgerminoma, especially those of Meyer, great stress was laid upon its frequent occurrence in pseudohermaphrodites and patients with sex underdevelopment of one type or another. That this association is a common one is undoubtedly true, as is the fact that disgerminoma is the most common tumor of pseudohermaphrodites, as it is of males with cryptorchidism. As cases have accumulated, however, it has become more and more evident that a large proportion, more than one-half, have occurred in ostensibly normal women. Klasten,⁶ for example, collected 30 such cases up to 1934, and a good many have been reported since then. In our own series of 17 cases, in 3 there was evidence of underdevelopment of the external or internal genital organs. In 1 of these there was primary amenorrhea, in another the uterus was absent, and in another it was very rudimentary, menstruation never having occurred in any of these 3 patients. In most of our cases no note was made as to the appearance of the involved ovary, but in several it was described as small and hypoplastic.

In 4 other cases hirsutism was observed, and in 2 was associated with enlargement of the clitoris, and in 1 with a deep, masculine type of voice. This last patient was obliged to shave daily. In this group, therefore, there is reason to believe that the disgerminoma developed in patients with at least mild degrees of pseudohermaphroditism. On the other hand, the mere presence of hirsutism in itself is not to be looked upon as indicative of intersexuality, as it is not infrequently noted in women who otherwise are quite feminine, and who perhaps menstruate and bear children quite normally.

The developmental abnormalities, when they occur, may therefore be of various types and grade. Three instances are reported in cases of true hermaphroditism (Polano, Aschkanazy, Reverdin), a considerable group in pseudohermaphrodites, many with extreme hypoplasia of the ovaries (often with complete primary amenorrhea), many with poorly developed sex characters, or with constitutional or sexual infantilism.

On the other hand, there have been a number of reports of disgerminoma in patients who have borne children before or after the operations for removal of the tumors. One of Kleine's patients⁸ had had 3 children before the operation, another two years after operation. Von Szathmáry¹³ reports 1 patient operated upon during pregnancy, and 1 during the puerperium. A number of other instances of pregnancy have been recorded, and to these we may add several from our own series. Three of our patients had borne 4, 2, and 2 children, before the development of the tumor, and 2 had children after operation, 1 patient having 2 pregnancies.

have remained free of recurrence for intervals of from a few months to six years. A number of these, however, are so recent as to be of little value from the standpoint of end results. This group of 10 cases, for purposes of tabulation, we have designated as the clinically non-malignant group (Table I).

TABLE I. TABULATION OF 17 CASES OF DISGERMINOMA

CASE	AGE	COLOR	PREVIOUS PREGNANCIES	SEX CHANGES	CLINICAL MALIGNANCY	ASCITES	FOLLOW-UP
1	18	W	0	Underdeveloped. Never menstruated	Invasion Fallopian tube	0	Not traced
2	16	W	0	Normal genitalia. Amenorrhea 3 mo.	Malignant	250 c.c.	Large tumor mass right side in 6 months
3	22	W	0	Normal	Metas. other ovary	0	Not traced
4	15	B	0	Normal	Omentum adherent. Benign	0	Not traced
5	16	W	0	Normal	Benign	0	Well after 4 yr. 2 normal deliveries
6	31	B	4	Normal	Peritoneal implants	3500 c.c.	Died in shock
7	22	W	0	Normal	Benign	Mod. amt.	Well 6 years. One normal delivery
8	6	B	0	Long clitoris. Absent uterus	Malignant	0	Radiosensitive. Well 4 years
9	12	W	0	Normal	Benign	3400 c.c.	Well 2 years
10	38	W	0	Absent cervix and other ovary	Benign	0	Well 2 years
11	22	W	2	Shaved. Deep voice. Metrorrhagia	Benign	0	Well 2½ years. Voice and hair the same
12	19	W	0	Normal	Benign	0	Died of obstruction in 5 days
13	10	W	0	Much genital hair	Malignant	0	Died after 3 months
14	20	W	0	Hirsutism. Long clitoris. Amenorrhea	Benign	0	Well one year. Hair and clitoris the same
15	18	B	0	Normal	Benign	0	Well (recent case)
16	36	W	2	Normal	Benign	0	Well 7 months
17	23	W	0	Hirsutism. Long clitoris	Benign	0	Well (recent case)

In 6 of our patients there was evidence at operation of local infiltration, at times extensive, or of metastases to other organs, and this group is referred to in Table I as clinically malignant. In 1 case we have not been able to secure information as to the presence or absence of infiltration or metastasis. Three of these 6 clinically malignant patients are dead, 1 of postoperative shock, 1 three months, and 1 six months after operation. One patient, treated by incomplete operation

In all other cases removal of both ovaries and uterus would seem to us to be the preferable procedure. This would include cases in which there is infiltration to other pelvic structures or metastases to any of the peritoneal or retroperitoneal organs, or to the lumbar glands. In such extensive cases complete removal is often impossible, and post-operative radiation must be resorted to. Even in this group instances of survival and apparent cure for a period of years have been noted. Our Case 8 is a good example of this, and similar cases are reported by Meyer, Schiller and others.

The question of whether or not disgerminoma is to be looked upon as a radiosensitive tumor cannot yet be answered with any definiteness. Some, like Meyer, consider these tumors to be radioresistant, while Gruss and others think they are radiosensitive. Our Case 8 would lead us to join the latter group. In this patient only very incomplete removal of the tumor was possible and this was followed by amazingly rapid and bulky recurrence, with equally remarkable disappearance of the recurrent tumor after radiation. Reappearance of other recurrences has been followed each time by rapid disappearance after radiation, the patient being still in good condition four years after the original operation, though quite probably not cured, as a small pelvic nodule is still palpable on rectal examination.

There is still another problem to be considered with reference to radiotherapy in cases of disgerminoma; viz., Is it advisable to use postoperative radiation in unilateral tumors removed conservatively, i.e., by removal of only the adnexa of the involved side? We believe that in most instances it is not, chiefly because of the fact that such treatment, by destroying the function of the conserved ovary, is just about as radical as a complete operation in abolishing the reproductive function, the preservation of which is the chief justification of more conservative procedures. If future reproductiveness is to be disregarded, the complete operation, followed by radiotherapy, would certainly seem safer and more desirable than unilateral removal plus radiotherapy.

SUMMARY

This paper is based upon the study of 17 cases of disgerminoma of the ovary which we have observed in our laboratory. While hitherto only 72 cases have been recorded in the literature, reports of cases of this tumor are now multiplying so rapidly that it may be considered not an exceedingly rare tumor type. Because of the fact that neither gynecologists nor pathologists have become generally familiar with the clinical and pathologic characteristics of ovarian disgerminoma, these have been fully discussed in our paper, together with the histogenesis of the tumor. The microscopic picture is so distinctive that the diagnosis should rarely present any difficulty, certainly far less than with granulosa cell carcinoma or arrhenoblastoma, both of which present many possible histologic variations and gradations.

Hormone studies have been made in a considerable number of cases, with negative results so far as the finding of sex hormones in the blood and urine, or in the tumor tissue, is concerned. This bears out the clinical observation that this tumor is of sexually indifferent type, with no such influence upon the development of secondary sex characters as is exhibited by granulosa cell carcinoma and arrhenoblastoma. The fact should again be emphasized that when disgerminoma is found in hermaphroditic or pseudohermaphroditic individuals, the tumor has played no rôle in the production of the intersexual condition, which is most often of the congenital or chromosomal type. Removal of the tumor, therefore, has no effect upon the sex characters of the patient.

In only 1 case in the literature, that of Tietze,¹⁴ is there an apparent contradiction of the above statement. Tietze's patient, a girl of ten, exhibited precocious menstruation and puberty, and these manifestations disappeared after removal of the tumor. Such a syndrome is quite characteristic of granulosa cell carcinoma, although the pathologic examination of Tietze's tumor revealed what he considers an undoubted disgerminoma. It is difficult to explain this association except on the ground that somewhere in the tumor there might have been an associated island of granulosa cell carcinoma, as in the cases reported by Schiller,⁹ and Reifferscheid.¹⁵

Treatment.—The diagnosis of disgerminoma of the ovary is rarely made before operation, and surgery is certainly the proper plan of treatment. There is still considerable difference of opinion with reference to the extent of the operation, depending upon differing viewpoints as to the degree of malignancy of the tumor. The question is complicated by the fact that such a large proportion of the patients are very young, so that radical operation is fraught with the great disadvantage that future reproductiveness is abolished. This sacrifice is not so great as would appear on first thought, for the reason that such a large proportion of these patients are sterile both before and after conservative operation. And yet in a number of reported cases pregnancies have occurred, either before or after unilateral operations, as we have already discussed.

On the basis of what we have already said in discussing the malignancy of these tumors, it would seem to us that conservative unilateral operations should be limited to unilateral growths in which the capsule of the tumor is intact, and in which there is no evidence of infiltration or metastasis. The procedure suggested by Frankl¹⁶ of incising the other ovary to permit of more careful inspection for the presence of small tumors may be worthwhile, though it certainly does not exclude the possibility of microscopic tumor elements. For example, Reifferschied was able to demonstrate microscopic disgerminoma in the presumably normal other ovary of a patient with a large unilateral disgerminoma.

A CLINICAL EVALUATION OF STEREOROENTGENOGRAPHY OF THE FEMALE PELVIS*

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RECENT developments in roentgenologic methods have again made the pelvis a major point of interest in obstetrics. By these new methods we are able to study an unlimited number of pelves in contrast to earlier workers, who had only a limited collection of dry pelves as their material. The routine use of clinical pelvimetry and existing classifications of the pelvis, in spite of certain limitations, has resulted in marked improvement in obstetric practice. We feel, however, that roentgenologic studies will supplement present clinical methods and help overcome their deficiencies.

The pelvis is composed of several bones whose ossification occurs at different ages. They are arranged to form an irregular canal, and this structure is so situated that it is subjected to great mechanical stresses and strains. In addition, throughout the period of development, its component elements are affected by sex and growth hormones, metabolic and nutritional influences, and evolutionary forces. The resulting multiplicity of form is not surprising, and we have to deal with a structure which is probably subject to greater individual variation than any other structure in the body with the exception of the face. Evidence has been accumulated which suggests the need for reconsideration of methods of examination and description. A new approach to an old subject is a great aid to perception, however, enthusiasm must be guarded, and facts must be presented which prove manifest superiority before a change can be considered. This study presents the results of our experience with the stereoscopic x-ray method of study and the classification of pelves as proposed by Caldwell and Moloy.

The precision stereoscope used in this study differs from the ordinary stereoscope in that it is designed to produce an image which is an approximately exact reproduction in form and size of the original object. It is most easily explained by a brief description of the method of taking the pictures and viewing them. The patient is placed in a horizontal position, a folded sheet is placed under the small of the back, tilting the pelvis forward and giving a better view of the superior strait. A right-angled wooden rod, the horizontal limb of which carries two lead markers whose inner borders are 9 cm. apart, is put in position. The horizontal limb extends across the patient's lower abdomen just

*Read at a meeting of the New York Obstetrical Society, May 11, 1937.

Since these tumors arise from cells dating back to the undifferentiated phase of gonadal development, it is not surprising that an exactly similar tumor, the well-known seminoma, occurs in the testis. Nor is it surprising that disgerminoma exhibits no endocrine activity, being made up of sexually indifferent cells. In this respect it differs from the feminizing granulosa cell carcinoma and the masculinizing arrhenoblastoma. Disgerminoma is often observed in sexually underdeveloped or pseudohermaphroditic individuals, but it has nothing to do with the production of these sex abnormalities, which persist even after removal of the tumor.

While disgerminoma is undoubtedly a malignant type of tumor, there are marked variations in the degree of malignancy of individual tumors. The outlook is very favorable when the tumor is unilateral, with intact capsule, as shown in our own cases, since 9 of 10 such cases have remained well after operation. The results are much less favorable when the capsule has been broken through, with extensive infiltration of surrounding organs, and perhaps metastases. Even when there is considerable infiltration, with incomplete removal, some patients have been apparently cured by postoperative radiation, which we believe is a valuable adjunct in such cases. The general principles of the treatment of ovarian disgerminoma have been discussed in the paper, on the basis of what has been learned as to their varying malignancy.

In conclusion, we wish to express our warm appreciation to the following gynecologists and pathologists who have referred to us material for study, and who have kindly permitted us to include their cases in this report: Drs. W. W. Cross, Fresno, Calif.; Karl M. Wilson, Rochester, N. Y.; Nathan P. Sears, Syracuse, N. Y.; Hollis N. Allen, St. Louis, Mo.; B. F. Eckles, Galax, Va.; R. H. Jackson, Madison, Wis.; L. J. Tragerman, Rafe Chaffin and Elizabeth Larsson, Los Angeles, Calif.; and Otto Schwarz, St. Louis, Mo.

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A special chart was employed for recording data in the study of each pelvis, in which ample provision is made for recording variations in form and degree of all components.

In our first series we employed an ordinary stereoscope which produces some distortion of the image and does not permit of measurement, but can be used for typing and studying cephalopelvic relationships at term.

Sixty-seven cases were studied (Table I), the patients being selected because of relationships to dystocia, past or anticipated.

The striking features brought out are the high percentage of mixed forms illustrating the multiplicity of variation encountered in individual pelvis, and the wide margin of error in clinical classification. In every class there is an error of 50 per cent in typing which suggests that the criteria employed for the purpose are unreliable.

In the second series the patients were selected as admitted to the ante-partum clinic, and we conducted our study without knowledge of the clinical findings. With the precision stereoscope we typed and measured the pelvis and attempted a prognosis based on type, size, and weight of the fetus. The relationship existing between cephalic diameters and weight of the fetus, as described by Thoms, was employed, and is, we believe, accurate in the majority of cases but subject to some marked exceptions.

TABLE I. COMPARISON OF CLINICAL AND ANATOMICAL CLASSIFICATIONS

<i>Clinical Types</i>					
NORMAL 32	G.C.T.† 21	FUNNEL 4	G.C. FUNNEL* 2	FLAT 7	FLAT FUNNEL 1
<i>Proposed Classification</i>					
GYNECOID 29	ANDROID 19	ANTHROPOID 7	FLAT 12		
<i>Reclassification of the 67 Pelves Showing the Variation From the Clinical Typing</i>					
	GYNECOID	ANDROID	ANTHROPOID	FLAT	
Normal (32)	17	5	4	6	
G.C.T. (21)	10	6	3	2	
G.C. funnel (4)	1	2	0	1	
Funnel typical (2)	1	1	0	0	
Simple flat (7)	0	4	0	3	
Flat funnel (1)	0	1	0	0	
Pure forms (Proposed classification)		36			
Mixed forms (Proposed classification)		31			

*G.C. Funnel, generally contracted funnel.

†G.C.T., generally contracted typical.

The percentage of occurrence of the various forms is of interest, and should reflect the average occurrence in our material (Table II).

TABLE II. OCCURRENCE OF PURE AND MIXED FORMS WITH PERCENTAGES
TOTAL NUMBER STUDIED 200

	TOTAL	PER CENT	PURE	PER CENT	MIXED	PER CENT
Gynecoid	124	62.0	76	38.0	48	24.0
Android	37	18.5	7	3.5	30	15.0
Anthropoid	23	11.5	4	2.0	19	9.5
Flat	16	8.0	4	2.0	12	6.0
Total	200	100.0	91	45.5	109	54.5

above the symphysis in such a way that the image of the markers appears on the x-ray film. The tube is centered on the midpoint of a line connecting the anterior superior spines. The tube film distance is 25 inches. One exposure is made, the tube then is shifted sagittally $2\frac{1}{2}$ inches, and the second exposure is made. In addition to the stereo films a lateral view of the pelvis is secured as well as a view of the symphysis and anterior wall of the pelvis.

The stereo films are placed in the viewing boxes, which are 50 inches apart, and at right angles to the line of vision through the optical apparatus. This establishes the 25-inch tube film distance for each viewing box. The images of the markers are plainly seen in a vertical plane in front of the pelvic image. The optical apparatus is then set so that the distance between the markers is 9 cm. We then have a reproduction of the conditions under which the picture was made, with the observer's eyes occupying the position formerly occupied by the x-ray tube. All images now seen should be approximately exact reproductions in form and size of the originals, and measurements can be made of any of these images.

PROPOSED CLASSIFICATION OF CALDWELL AND MOLOY

Fortunately this classification is based on only four parent types, all of which are familiar to us, as they are described as definite types in practically all of the old classifications.

The classification is based on the character of the superior strait. The posterior segment, or that portion which lies behind the greatest transverse diameter, is regarded as the dominant characteristic, and determines the type to which the pelvis belongs. The character of the anterior segment determines the accompanying tendency. In the pure types, the posterior and anterior segments correspond to the same parent type, whereas the mixed forms are made up of the possible combinations between the posterior and anterior segments of the four parent types.

The Gynecoid Type.—This is the normal female pelvis of other classifications. The superior strait is blunt heart shaped.

The Android Type.—These female pelvises strongly resemble the male pelvis, particularly in the posterior segment, and they correspond to the male type of other classifications. The superior strait is triangular in form.

The Anthropoid Type.—These pelvises bear a resemblance to the pelvises of the anthropoid apes and correspond to the transversely contracted pelvises of some classifications. The superior strait is roughly elliptical, with the long diameter anteroposterior.

The Platypelloid Type.—These pelvises correspond to the simple flat pelvises of other classifications. The superior strait is roughly elliptical, with the long diameter transverse.

The Asymmetrical Pelvises.—Aside from the asymmetry, these pelvises usually conform to one of the major groups listed.

All classes are subdivided on the basis of variations in size of the subpubic angle into those: (1) with a narrow outlet; (2) with a moderate outlet; (3) with a wide outlet; and (4) large and small.

TABLE V. THIRTY-FOUR PATIENTS WITH A CONJUGATA VERA OF UNDER 10 C.M., SEPARATED UNDER THE TWO CLASSIFICATIONS

	NORMAL	G.C.T.	G.C.	FUNNEL	FUNNEL	FLAT	G.C.R.
Gynecoid	8	0	1	0	0	0	14
Gynecoid with android	1	1	0	0	0	0	
Gynecoid with anthropoid	0	0	0	0	0	0	
Gynecoid with flat	2	0	0	0	1	0	
Android	1	0	0	0	1	1	13
Android with gynecoid	2	0	0	0	5	0	
Android with anthropoid	0	1	0	0	0	0	
Android with flat	0	0	0	0	2	0	
Anthropoid	0	0	0	0	0	0	0
Anthropoid with gynecoid	0	0	0	0	0	0	
Anthropoid with android	0	0	0	0	0	0	
Flat	0	1	0	0	1	0	7
Flat with gynecoid	4	0	0	0	1	0	
Flat with android	0	0	0	0	0	0	
	18	3	1	0	11	1	

PROLONGED LABORS

In Table VI we have analyzed the patients who had a labor of twenty-four hours and more, together with the operative incidence. The relatively low percentage of pure gynecoid pelves again stands out, and in these cases we could find nothing to account for prolonged labor. The operative incidence in the pure gynecoid group is also low.

TABLE VI. SUMMARY OF 33 CASES OF PROLONGED LABOR IN THE 200 CASES

Normal pelves clinically	78.8%	Gynecoid (normal by x-ray)	19.0%
		Gynecoid (mixed)	30.7%
		Android (pure and mixed)	18.7%
		Anthropoid (pure and mixed)	13.0%
		Flat (pure and mixed)	18.6%
			100.0%
Operative incidence	33%		
		Gynecoid (pure)	11.0%
		Gynecoid (mixed)	33.3%
		Android (pure and mixed)	33.3%
		Anthropoid (pure and mixed)	11.2%
		Flat (pure and mixed)	11.2%
			100.0%

The android group is again prominent both in relative percentage occurrence and in operative incidence. The android or male pelvis was not recognized clinically in this group.

The flat pelvis was not correctly diagnosed clinically in a single instance. Its occurrence in the group was the same as that of the android, and the operative incidence in this group was just one-third that of the android. The android again gets a first place award for trouble and for traveling incognito.

In Table VII we have analyzed the cases which came to cesarean section. Attention is directed to the incidence of android pelvis in this group. The x-ray prognosis was based on a study of the pelvis alone, and we feel that this practice, while of distinct value, should be replaced by studies of cephalopelvic relationships at term in all questionable cases.

The percentage of occurrence of the various forms approximates those reported by Caldwell, Moloy, and D'Esopo in a similar series.

We thought it significant that pure types exceeded the mixed forms in the gynecoid group alone.

Percentage of occurrence of various forms will vary in different series according to race, and probably will also be found to be influenced by social and economic status.

Table III shows the percentage of occurrence of normal pelves according to clinical classification and the reclassification of these same pelves; 86.5 per cent were called normal, whereas only 36.5 per cent were pure gynecoids.

Contracted pelves, according to clinical classification, constituted 27 or 13.5 per cent. The occurrence of various types and their classification are shown in Table IV. In this table we again see a gross error in typing, and it is also significant to find such a large percentage of android forms unrecognized.

TABLE III. NORMAL PELVES IN CLINICAL CLASSIFICATION (173)

THESE CLASSIFIED ACCORDING TO PROPOSED METHOD					
Gynecoid	73	} Gynecoid (pure) Gynecoid (mixed)	73	} 113	
Gynecoid with android	18		40		
Gynecoid with anthropoid	13				
Gynecoid with flat	9				
Android	4	} Android (pure) Android (mixed)	4	} 24	
Android with gynecoid	16		20		
Android with anthropoid	4				
Android with flat	0				
Anthropoid	4	} Anthropoid (pure) Anthropoid (mixed)	4	} 23	
Anthropoid with gynecoid	18		19		
Anthropoid with android	1				
Flat	2	} Flat (pure) Flat (mixed)	2	} 13	
Flat with gynecoid	11		11		
Flat with android	0				

TABLE IV. CONTRACTED PELVES

	GYNECOID		ANDROID	ANTHROPOID		FLAT
G.C.T.	7	5	1	0	1	} 4
Simple flat	15	3	8	1	3	
Funnel typical	2	2	0	0	0	
G.C. funnel	2	1	1	0	0	
G.C.* rachitic	1	0	1	0	0	
Contracted	27					

*G.C., generally contracted.

In Table V we have arranged, according to both classifications, all pelves with a true conjugate under 10 cm. as measured by x-ray methods. Eighteen supposedly normal pelves with a C.D. of 11.75 and over fell into this group. Actually only 50 per cent of this number were found to be true normals according to accepted clinical criteria.

When we consider the large percentage which the gynecoid group constitutes in the total series, namely, 62 per cent, the occurrence of this type of small pelvis is quite low and in marked contrast to the android type which has the same incidence and constituted only 18.5 per cent of the series, a ratio of 3 to 1. The anthropoid types were not found as would be expected because of the relatively long anteroposterior diameter. The flat type clinically made up 32.4 per cent of the group, whereas actually they only constituted 20.5 per cent. Three-fourths of them proved to be android. Only one pelvis was typed as male, and this proved to be a normal female, with a narrow outlet.

of 3,900 gm. It would seem that this is a logical explanation for the absence of pelvic dystocia in 85 per cent of all cases.

Pelvic architecture and size become significant only when the fetal head approximates the size of the pelvis, or the diameters of the fetal head are larger than the pelvic diameters. An oversized head in a normal pelvis means trouble, and a variation in architectural form in such a situation exaggerates the difficulty. The varying forms, we believe, have a varying significance.

OBSTETRIC SIGNIFICANCE OF THE PARENT TYPES

The gynecoid type constitutes 62 per cent of the total and occurs most frequently in the pure form. The pure forms were associated with only one operative delivery.

The android type, male type of other classifications, is easily the most dangerous type encountered. Although it constituted only 18.5 per cent of the total material, it was found to be associated with 80 per cent of the cesarean section cases; 33 $\frac{1}{3}$ per cent of the remaining operative cases; 18 per cent of the prolonged labors; and 38 per cent of the small pelves.

Male pelves are diagnosed clinically as male or funnel pelves and this diagnosis is usually based on the presence of a contracted outlet. In the cases having this type of pelvis which encountered serious difficulty, the pelvic type was not diagnosed in a single instance; furthermore, the inlet was the important factor in this situation. We do not feel that it is possible to diagnose accurately the presence of this type of pelvis by the clinical methods usually employed.

The anthropoid type: Due to the relative transverse contractions of the inlet, engagement is frequently delayed until the fetal head is adjusted to the long anteroposterior diameter. With the head in the transverse diameter, disproportion on abdominal examination seems evident, whereas actually when adjustment occurs there is ample room. Knowledge of the transverse contraction is important in forestalling ill-advised attempts to rotate an anteroposterior position and in bringing an aftercoming head into the pelvis in the anteroposterior diameter. Because of the relative and actual increase in the anteroposterior diameter we seldom suspect a variation from normal in the clinical examination of these pelves. In this series they occurred 23 times and were all listed as normal.

The platypelloid group or flat group: This type represented 8 per cent of the total series. It corresponds to the simple flat pelvis of other classifications. In the group which had true conjugates under 10 cm. there were 7, a percentage of 20.5 of the group of small pelves (Table V). Fifteen flat pelves occur among the clinical group of contracted pelves, whereas we only placed three of these in this category. In nearly all cases they were confused with the small android pelvis. This is highly misleading because the prognostic outlook in the android pelvis is very bad, whereas that in the flat pelvis is very good, unless the contraction is of extreme degree, or other complicating factors exist. The flat pelvis gave rise to no serious difficulties which is significant in view of their relatively high incidence of occurrence in the group of small pelves. This stands out in marked contrast with the android group.

CEPHALOPELVIC RELATIONSHIP AT TERM AND IN LABOR

In a series of 40 pelves, we studied the relationships of the head and pelvis at term. We recorded measurements of the head and

TABLE VII. CESAREAN SECTION

CLINICAL CLASSIFICATION	C.D.	PROGNOSIS	X-RAY CLASSIFICATION	C.V.	PROGNOSIS	OUTCOME AND PREVIOUS LABOR
G.C.R.	8	Elective cesarean section	Android	6.1	Elective cesarean section	Cesarean section 3,160 gm. Para v. All cesarean sections
Normal	11.75	Trial labor. Good chance for normal delivery	Android with gynecoid	10	Trial labor. Probable section for large baby	Cesarean section low. Flap after 19 hours. 4,220 gm. Former cesarean section for 3,520 gm. baby
G.C.T.	11.5	Elective cesarean section	Gynecoid with android	9.4	Good for 3,600 gm. Posterior position	Elective cesarean section. 3,800 gm. 1st labor 33 hr. R.O.P. mid-forceps 3,600 gm. baby
Simple Flat	11	Spontaneous outcome, then cesarean section	Android with gynecoid	9.3	Good for 3,100 gm. Section if over. O.P. position	Latzko after 48 hr. 3,550 gm. R.O.P.
Normal	12	Lesion in cervix may cause dystocia	Android with gynecoid	9.5	Good for 3,500 gm.	Cesarean section after 64 hr. Cervical dystocia. R.O.T. 3,350 gm.

Prognosis was actually 80 per cent correct. In the last case the indication for cesarean was cervical dystocia due to a definite lesion in the cervix. In the presence of an android pelvis we feel that such a diagnosis may be questioned.

DIAGONAL CONJUGATE

In the clinical classification of pelvis, the length of the C.D. has been used as the most important factor in determining the type. It has long been known that the C.V. does not bear a constant relationship to the C.D. but for clinical purposes we have come to subtract 2 to $2\frac{1}{2}$ cm. from the C.D. to estimate the C.V. The fallacy of this practice is borne out by Table VIII which shows that in 200 pelvis, 147 do not fall into the above group.

TABLE VIII. OBSERVATIONS ON THE C.D. OR DIAGONAL CONJUGATE

In 11 pelvis the C.D. exceeded the C.V. by more than $2\frac{1}{2}$ cm.
In 89 pelvis the C.D. exceeded the C.V. by 1 to $1\frac{3}{4}$ cm.
In 29 pelvis the C.D. exceeded the C.V. by $\frac{1}{4}$ to $\frac{3}{4}$ cm.
In 8 pelvis the C.D. was equal to the C.V.
In 10 pelvis the C.D. was less than the C.V.

THE AVERAGE MARGIN OF SAFETY BETWEEN HEAD AND PELVIS

The average weight of babies born in our clinic is 3,360 gm. We find the average pelvis including all classes will accommodate a fetus

TABLE X. TYPE OF PELVES IN 12 PATIENTS WHO HAD CESAREAN SECTIONS

Gynecoid	2
Gynecoid with android	1
Gynecoid with anthropoid	2
Android with gynecoid	2
Android with flat	3
Flat	1
Flat with gynecoid	1

We thought the work Table X of the 40 cases on which the above is based would be of interest.*

SUMMARY AND DISCUSSION

The routine use of classification of the pelvis and clinical pelvimetry have played an important role in the improvement of the end results in modern obstetrics. It has, however, long been realized that they were both inadequate and subject to considerable inaccuracy.

Previous classifications have not made provision for the very frequent occurrence of variations in the component elements of the pelvis resulting in the so-called mixed types. In the pelves which we studied and in much larger series, these mixed types constituted approximately 50 per cent of the total. On the basis of 4 parent types, all of which are recognized in practically all classifications, the possible combinations in form and size total up to 96. When such a multiplicity actually exists it is manifestly impossible to describe individual pelves accurately by adherence to any reasonable number of types.

In the clinical examination of the pelvis, we are definitely limited in our study of the canal and superior strait. The diagonal conjugate is an indirect measurement of the anteroposterior diameter and subject to a very variable relationship to the true conjugate, and in addition yields very little information about the conformation of the superior strait. The transverse diameter of the outlet is not an accurate criterion for classifying pelves as one may encounter any type of outlet associated with any one of 16 types of inlet.

Eighty-five to 90 per cent of all labors present no problem of pelvic dystocia. In the remaining 10 to 15 per cent, varying degrees of difficulty are encountered. In 3 to 5 per cent of the latter abdominal delivery is necessary.

The incidence of contracted pelves in a large series of cases is reported to be from 8 to 24 per cent, averaging 16 per cent. This figure corresponds to the number of women encountering pelvic dystocia; when the cases are analyzed, however, we find that the two groups do not correspond for there are many in the dystocia group in which the pelvis was thought to be normal, and many in the contracted pelvis group who have encountered no difficulty. In addition, the type of pelvis seemed to be an important factor and the type had not been recognized clinically in an appreciable number.

The employment of a method which permits of direct inspection of the pelvic canal, a study of cephalopelvic relationships at term, and

*For lack of space this table can only be included in the authors' reprints.

pelvis, and gave a prognosis on the outcome. This was done on patients near term or in labor in whom difficulty was expected or was being experienced.

TABLE IX. PELVES STUDIED AT TERM—CLASSIFICATION

	NORMAL	SIMPLE FLAT	G.C.T.	G.C.R.	FLAT RACHETIC	FUNNEL TYPICAL	TOTAL
Gynecoid	7	3	1	0	0	0	11
Gynecoid with android	0	0	0	0	0	1	1
Gynecoid with anthropoid	3	1	0	0	0	0	4
Gynecoid with flat	0	1	0	1	0	0	2
Android	0	0	0	0	0	0	0
Android with gynecoid	1	1	2	0	0	0	4
Android with anthropoid	0	0	0	0	0	0	0
Android with flat	1	1	0	0	1	0	3
Anthropoid	0	0	0	0	0	0	0
Anthropoid with gynecoid	1	1	0	0	0	0	2
Anthropoid with android	0	0	0	0	0	0	0
Flat	1	3	0	1	0	0	5
Flat with gynecoid	0	5	0	0	0	0	5
Flat with android	2	0	0	0	0	0	2
Total	16	16	3	2	1	1	39

1 Android with flat, unclassified

Twelve cesarean sections were performed in a group of 40 cases, 1 for acute yellow atrophy, and 2 for previous cesarean section with febrile puerperium. This leaves 9 sections done for cephalopelvic dystocia. Of these, 6 were predicted by x-ray studies. Of the 3 not predicted, one was a patient with a flat with gynecoid type of pelvis, true conjugate 8.75 cm. We estimated the biparietal diameter of the baby at 9 and the weight at 3,500 gm. They were 9 and 3,550 gm., respectively, and in favor of the spontaneous outcome was the fact that the patient had delivered a 3,550 gm. baby through the vagina. The second was in a patient with an android with gynecoid pelvis and a posterior parietal presentation. This was diagnosed by x-ray and a long labor with possible section was predicted. Vaginal delivery was thought doubtful. A low cesarean section was done after fifty-seven hours of labor. The third was in a patient with a gynecoid type of pelvis whose C.V. was 10.5 cm. and C.D. 10.25 cm. By x-ray it was felt that she could deliver a 3,600 gm. breech. The baby obtained at section was a breech, weighed 3,010 gm. and had a biparietal of 9.75 cm. This type of pelvis in which the C.V. approaches the C.D. will always be missed by the present clinical methods. We feel confident that two of these three patients could have been delivered vaginally. One trial labor and probable section predicted by x-ray was not done. The patient had a short, easy labor.

In our estimate of biparietal diameters our average error was 0.15 cm., and except for one case of 1 cm. variation, our greatest error was 0.5 cm. Molding, naturally, alters the measurements of the head and prevents an accurate post-partum check of the x-ray estimates. Our average error in weight estimation was 168 gm., and our greatest error 870 gm.

In this group of 40 cases there were 17 prolonged labors, 2 of which had sections, and 10 additional sections, making 27 cases out of 40 who had sections or prolonged labor. Five dead babies, or 12 per cent fetal mortality was obtained. Cross classification of these 40 cases by clinical and x-ray methods is shown in Table IX.

In Table X is shown the type of pelvis in the 12 patients who had cesarean sections. The 3 done for nonpelvic reasons were in a gynecoid, a gynecoid with android, and a gynecoid with anthropoid.

considerable expense and could yield useful information in only a small percentage. As an adjunct in the management of labor we suggest the examination near term of those patients in whom dystocia is anticipated, and examination during labor of those in whom dystocia develops which has not been anticipated.

The routine employment of the Roentgen ray in the examination of pregnant women is a question for the future. It is employed in at least one clinic in this country, and we feel that to insure accuracy in classification, it will have to be considered. In other fields we have witnessed an increasing use of this means of examination. Any doctor treating fractures today would not dare to omit the use of the Roentgen ray. The same is essentially true in the fields of pulmonary tuberculosis, gastroenterology and neurosurgery.

This study has been limited to an investigation of the Caldwell and Moloy classification of pelves and the stereoroentgenographic method of study. Several new methods of investigation have appeared in the last few years and as a result, new classifications have been proposed. Comparison of all methods is very much in order, and it is felt that modification and combination in investigation and description will eventually result in the adoption of the most valuable procedures.

Clinical pelvimetry and the classification of pelves by existing methods constitutes one of the foundation stones in obstetrics. Our observations raise serious questions regarding the accuracy and adequacy of the ordinary mensuration method. However, changes cannot be considered unless other workers corroborate our findings after studying large series of pelvic roentgenograms. In the event of confirmation, could we afford to neglect the use of an agency that offers improvement in our basic structure?

CONCLUSIONS

1. We believe the Caldwell and Moloy classification of the female pelvis based on a stereoroentgenographic study should prove to be more accurate than any clinical classification now in use.

2. The stereoscopic method of study is essential for accurate classification of the pelvis, and provides at the same time an additional and reliable means of measurement.

3. Cephalopelvic relationships at term and during labor may be accurately observed and a prognosis given independent of measurements.

4. Pelvic architecture, per se, as a factor in dystocia deserves more consideration than it has received.

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which gives a high degree of accuracy in measurement, would seem to offer a valuable adjunct to our present methods. The classification offered is one which provides for an accurate description of individual pelvis, and is based upon only four parent types all of which are familiar because of their inclusion in previous classifications.

The clinical typing of pelvis is subject to considerable error which raises a question about the evaluation of the pelvis as a factor in dystocia based on clinical studies.

The diagonal conjugate has a very variable relationship to the true conjugate, and is open to question as a guide in typing and as a basis of judgment in prognosticating outcome in an appreciable number of cases.

The shortened transverse diameter of the outlet is practically the sole criterion for recognition of the male type pelvis. This diagnostic sign may be present in any of the pelvic types and hence of little value as a criterion. The study of the sacrosciatic notch by palpation may give a hint to the observer, but our experience to date with this procedure has not been encouraging, and we feel that it is a moderately painful procedure in the average primigravida.

In the cases we studied, the male type of pelvis was not recognized, clinically, except where there happened to be an accompanying contracted outlet, and in the cases which developed dystocia, the trouble occurred at the inlet.

The transversely contracted pelvis was not diagnosed clinically in a single instance.

In the group of flat pelvis, cesarean sections were done which we feel from the results of our examination, had an excellent chance to deliver per vaginam.

These fundamental defects are corrected by the employment of the stereoroentgenographic method of pelvimetry. The prognostic accuracy which we obtained in the longer series when the prediction was based on pelvic type alone, and in the shorter series where we predicted type of delivery as well as cephalic measurement and weight of the fetus, compares very favorably with clinical prognosis. With the attainment of some background of experience, and the employment of this method along with a full clinical knowledge of each patient, much guesswork should be eliminated.

In addition, we are offered an unprecedented opportunity to study the mechanism of engagement, the mechanism of labor, and to find out the actual role of the pelvis as a factor in dystocia.

The classification of pelvis proposed by Caldwell and Moloy is simple and comprehensive, and offers a possible solution of an accurate descriptive terminology for the extremely variable forms presented by nature.

Many obstetricians have asked the question, do you propose to have an x-ray of every patient? It is conceded by all that there are only 15 per cent of all cases in which any question regarding the pelvis will arise, and probably only one-half of these will encounter serious difficulty. Manifestly an x-ray of every patient would entail

protein diet were able to hold the normal cholesterol and urea nitrogen ratio, and they were notably free from edema (Table II).

TABLE II

MRS. L.L. AGED 35, PARA III. EIGHT MONTHS PREGNANCY. MODERATELY EDEMATOUS

DATE	BLOOD UREA NITROGEN	CHOLESTEROL	TOTAL PROTEIN	SERUM ALBUMIN	CHLORIDE	CARBON DIOXIDE	HEMATOCRIT	POTASSIUM	REMARKS	
6/21	10.3	410	5.09	3.13	490	39.3	50.0	20.7	High protein diet.	5 gm. KCl
6/28	12.5	303	5.14	3.60	480	36.2	47.6	23.1	High protein diet.	5 gm. KCl
7/ 5	14.3	290	7.81	3.40	530	35.3		23.4	High protein diet.	5 gm. KCl
7/12	17.2	255	7.50	2.85	510	36.6	44.7	21.9	Normal delivery.	No edema.

Table II shows blood findings of patient late in pregnancy with generalized edema.

The low urea and increased cholesterol return to essentially normal figures when given a high protein—low sodium—high potassium—acid ash diet with potassium chloride as a salt substitute.² Beginning on the fourth day, the edema rapidly disappeared. Note the falling carbon-dioxide combining power indicating necessity for careful supervision.

It is interesting to recall that similar blood pictures were produced in dogs by diets adequate in calories, minerals, and vitamins but deficient in protein. It is also important that if the protein restriction was great and continued over a period of time, the cholesterol began to fall and the animals died of marked fatty infiltration and degeneration of the liver.³ Dieckmann's excellent work⁴ has brought out the grave prognosis associated with a decreasing cholesterol in the toxemias of pregnancy.

Thus, one large group of pregnant women were thought to be on inadequate protein diets. When they were fed liberally of protein rich foods, an improvement of strength, loss of the pasty appearance and decrease of the edema were noted. Convalescence seemed to be materially shortened by the improved nutritional state.

Unfortunately all pregnant women who may show protein deficit as evidenced by a low urea and a high cholesterol reading in the blood are not able to eat meats without producing symptoms. It has long been known by obstetricians that so-called toxemias of pregnancy might be averted or benefited by rigid protein restriction.

A study of all types of cases entering the clinic and the associated hospitals showed additional blood patterns which are thought to be of significance in relation to the need for protein restriction. A small percentage of the total cases showed, late in gestation, a normal or slightly elevated blood urea nitrogen, a mild elevation of the cholesterol and a normal carbon-dioxide combining power, but the uric acid, and phosphorous content of the blood were increased. These patients often showed slight elevations of the blood pressure and some urine specimens might contain albumin. Dizziness, spots before the eyes, and headaches were occasionally mentioned. Generally speaking, no trouble was ex-

BLOOD CHEMISTRY OBSERVATIONS IN PROTEIN DEFICIENT AND TOXIC PREGNANCIES*

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DURING an investigation of cholesterol metabolism of pregnancy¹ I noted various patterns of nitrogen, mineral, and acid base equilibrium of the blood. The chief findings in about one-half of the pregnant women showed a low blood urea nitrogen and a high cholesterol, but the uric acid, phosphates, sulfates, chlorides, carbon dioxide combining power, and other blood chemical determinations were normal or irrelevant. A series of women were studied from the early months of pregnancy and in general, during the second trimester of pregnancy, the blood urea nitrogen began to fall and this was followed by a rise of the cholesterol. A dietary review showed that these shifts were in fairly close relation to the total protein intake. Specific questioning brought out the lack of meat, eggs, milk, and cheese in the diet. Many women lived almost entirely on bread, vegetables, fruit, coffeecake, and coffee. The lay fear of eating meat during pregnancy, fear of getting fat or developing too large a baby were common reasons given for omission of protein rich foods. Such protein-poor diets were found in about 50 per cent of both clinic and private patients. The dietary review proved to be a good index of the degree of low blood urea nitrogen and the hypercholesterolemia which would be found (Table I).

TABLE I

PATIENT	HB	UREA	URIC	PO ₄	CL.	CO ₂	CHOL.
S.R.	36.0	9.3	2.35	2.63	488	51.6	260
B.N.	36.0	9.7	2.96	2.90	480	50.2	296
M.R.	39.0	7.8	2.75	2.60	476	50.7	310
S.R.	32.8	7.0	2.80	2.92	520	57.0	388
L.M.	39.0	8.8	2.55	2.66	480	56.0	370

As pregnancy advanced this group of patients generally grew a little more pasty and sallow, and they were troubled with increasing puffiness of the face and edema of the extremities. A definite hydremic plethora was indicated by the reduced red count, hematocrit and total serum protein. The blood pressure was generally normal or low and the urine was free from albumin until late when an occasional patient might well show both albumin and casts of moderate degree. When these patients were given a liberal or high protein diet of meat, eggs, milk, and cheese, the blood urea nitrogen was raised toward normal and the blood cholesterol was held to its level or gradually decreased. Patients that took a liberal

*Read at a meeting of the Chicago Gynecological Society, May 12, 1937.

chemistry findings, and these observations suggest the need for such laboratory assistance as described as an index to better evaluation and dietary therapy of those who need protein in contrast to those whom proteins may well destroy. The few "toxic" cases that have been given a rigidly low phosphorous-alkaline ash diet with calcium carbonate and potassium citrate sufficient to combat the acidosis, have done sufficiently well to warrant further study.

Although these observations have been recorded by many workers in the past,^{5, 4, 6} etc., it is hoped that others may be interested in checking some of the interpretations which have been made in this paper, which are:

1. A large group of pregnant women are benefited by a very liberal protein diet.

2. A few second and third trimester women are endangered even by small amounts of protein.

3. Simple, well-established blood chemistry tests may differentiate these groups and serve as a guide to better dietary and therapeutic control.

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DISCUSSION

DR. W. J. DIECKMANN.—We have described the marked and sudden alterations in blood and plasma volume which occur simultaneously with changes in the clinical symptoms and signs. These changes in blood volume, as depicted by alterations in the concentration of hemoglobin, serum protein, and cell volume, are of diagnostic and prognostic value.

The internist, in his study of vascular-renal disease, has some advantage over the obstetrician in that the disease is of long duration. However, pregnancy toxemias are quite often ideal cases of research, because one can study the normal and abnormal in the same patient over a relatively short period of time. Dr. Barker has remained conservative in his conclusions. I deplore, however, the assertions of one internist that pyelitis is an important factor in toxemia and the statement of another that a high protein diet will prevent eclampsia.

Dr. Barker states that protein is toxic to certain groups of pregnant patients. Obstetricians have learned this by bitter experience and have been using this knowledge for several decades. I do not hesitate to give protein to a large number of toxemic patients but I do not give it to all. Our standard preeclamptic diet contains 60 gm. of protein. We have attempted to give certain toxemic patients 100 to 150 gm. protein per day but so far, none of the 25 patients would take all of the protein. Furthermore, our results with forced protein feeding have not been so good as with our usual treatment.

Our chemical data are essentially similar to Dr. Barker's. We have not been able to increase the blood urea by protein feeding and have been attempting to determine for the past seven years why the blood urea is lowered in pregnancy.

I believe that within the next few years after sufficient chemical and clinical data have accumulated, someone will group it properly and the mystery of eclampsia and allied conditions will be explained.

perienced and the greater part of this group went to normal deliveries without a symptom (Table III).

TABLE III

PATIENT	HB	UREA	URIC	PO ₄	CL.	CO ₂
Y.K.	48.0	16.2	3.90	3.16	470	56.0
G.N.	32.0	15.5	3.18	4.80	488	52.0
T.R.	47.0	19.2	3.48	4.42	504	49.6
P.S.	42.0	17.7	4.55	4.25	472	51.0
O.J.	32.0	13.3	4.50	4.56	508	40.9

Finally, an occasional patient showed a similar picture of normal or slightly elevated blood urea nitrogen and a slightly increased to decreased cholesterol, but the uric acid and phosphorus were greatly elevated in the blood and a sharp acidosis was indicated by the low carbon-dioxide combining power. This group (12 patients) all had eclampsia. All but two showed albumin in the urine. Two had typical convulsions without premonitory symptoms or elevations of the blood pressure. Two had detached retinæ, loss of memory, etc., for many weeks. Blood findings on five of these patients are shown in Table IV.

TABLE IV

PATIENT	HB	UREA	URIC	PO ₄	CL.	CO ₂
L.K.	30.0	16.1	8.90	4.45	492	39.2
G.N.	33.0	15.0	6.10	4.42	508	41.0
B.L.	36.0	24.0	6.25	4.83	524	43.8
R.C.	43.0	20.0	5.25	4.55	526	38.8
R.R.	27.0	22.8	12.00	5.70	532	13.6

The fifth patient showed a uric acid of 12.0, a phosphate of 5.70, and a carbon dioxide of 13.6. Needless to say that this unfortunate patient died.

DISCUSSION

These findings fall roughly into three groups. The greater number (Group I) show a low urea nitrogen and a high blood cholesterol with a normal uric acid and blood phosphate. These patients seem to do much better on a diet sufficiently rich in protein to maintain a urea cholesterol ratio below 20 to 1. (Urea over 12 and cholesterol below 240.) Another (Group II) who may likewise appear pasty and edematous may, even with a normal blood pressure, seem unable to clear the waste products of protein metabolism. Certainly they store up phosphorus, the uric acid increases and an acidosis develops. If this is allowed to progress, the eclamptic syndrome may follow (Group IV). (The greatest source of phosphorus and other acid forming foods is the proteins, whole wheat bread, oatmeal, eggs, etc., and our limited experience indicates that they should be rigidly restricted just as advocated by obstetricians for many years.) The possibility of some low renal reserve as Stander⁵ has emphasized or some other fault in protein metabolism or mineral clearance seems to enter into the problem of this eclamptic group. Certainly the patients who may look the same externally may have very different blood

MASCULINIZING ELEMENTS IN THE OVARY*

RALPH A. REIS, M.D., AND OTTO SAPHIR, M.D., CHICAGO, ILL.

(From the Departments of Gynecology and Pathology of the Michael Reese Hospital)

TRUE masculinizing tumors of the ovary are rare. A study of the comparatively few reports in the literature shows a diversity of opinion both as to the structure and the origin of these tumors.

There are three types of tumors which are linked with the syndrome of masculinization. The first of these, the so-called arrhenoblastoma or andreiblastoma¹ has received much attention. This tumor is said to arise from misplaced testicular structures located within or close to the ovary. In the latter, the invasion of the ovary is secondary. Whether such a tissue growth may be considered a true neoplasm or merely the result of a primary malformation resulting in the individual being classified as an intersex or hermaphrodite, depends upon a study of the entire body.

The second type of ovarian tumor which may give rise to masculinization is the disgerminoma. This tumor is said to arise from early gonad cells before such cells have been differentiated into either ovarian or testicular structures. There are, however, a number of disgerminomas reported² without any symptoms of masculinization.

The third type of ovarian tumor in this masculinizing group arises from misplaced suprarenal cortical cells according to most authors.³ Neumann has used the term, "interrenalism," for the symptoms which follow the development of such masculinizing tumors. Interrenalism, according to Neumann, implies (a) disturbances of sex functions such as oligomenorrhea, hypomenorrhea, infertility or sterility, loss of libido and hypertrophy of the clitoris, (b) changes in the secondary sex characteristics such as hypertrichosis and the development of the deep virile voice, and (c) adiposity and virile musculature; cachexia may develop as a terminal change.

The genesis of this tumor is not clear. Most authors⁴ believe that it arises from misplaced suprarenal cortical rests within the ovary and therefore term this tumor hypernephrotic tumor, hypernephroma or Grawitz tumor, similar to those which are found in the kidneys. This view is supported by the fact that suprarenal cells are occasionally found in the ovary. Furthermore, it is known that a primary tumor of the suprarenal cortex occurring in female children will produce virilism and pubertas precox.

There are, however, investigators⁴ who believe that these tumors arise from lutein cells of the ovary and therefore designate them as luteomas. It is a fact that these tumor cells do resemble lutein cells, and according to Masson,⁵ a fine reticulum network similar to that seen in the corpus luteum is recognizable within this type of tumor. Such a reticulum cannot be found in the tumors which arise from the suprarenal cortex. Furthermore, Schiller⁶ states that luteinization of granulosa cell tumors may lead to masculinization. Hochloff⁷ called his tumor a hypernephroma of the ovary, but Kermauner⁴ believed that this tumor might equally well have been called a lutein cell blastoma.

This short survey shows the confusion which exists in regard to this type of ovarian tumor. On theoretical grounds, both tumors, the hypernephroma and the lutein cell blastoma, may give rise to the symptoms of masculinization. Anatomically, however, it is not possible to differentiate between lutein cell blastoma and hypernephroma.

*Read at a meeting of the Chicago Gynecological Society, May 21, 1937.

DR. E. L. CORNELL.—I can corroborate everything Dr. Barker has said relative to the use of protein diet. He did not mention that the blood pressure increases with the decrease of urea and increase of cholesterol in the average patient. The edema, blood pressure, and blood chemistry practically are parallel. If the sodium radical, whether in food, baking soda, or table salt, is decreased at the same time the protein is increased, the edema will decrease very rapidly. I have seen private patients lose as much as 6 to 8 pounds in a week on ambulatory treatment.

From a clinical standpoint, I doubt if you can apply the line of treatment to every patient who shows signs of toxemia. I am not entirely satisfied that the increase in protein and decrease in the sodium radical will handle all patients. It will control the majority of mild toxic patients we see in the average practice.

DR. FRED H. FALLS.—One must be very careful about feeding the preeclamptic patient protein. I think there is no question but that the toxin which is circulating in the blood of a woman with eclampsia comes from the protein molecule. It is a protein split product. It is the same protein toxin you find in anaphylactic shock. It is the same protein poisoning you find in the venom of the rattlesnake.

There are three sources of this toxin in the pregnant woman. One of the important sources is the food she takes in; the second is the breaking down of the body protein; and the third and most important is the alteration of function and metabolism of the placenta following circulatory disturbances. Those factors give rise to clinical eclampsia. If you have a slowly developing eclampsia it may be due to an indiscretion in diet, but in the fulminating type it is not due to the over eating of protein or to over exercise but is due to abnormal protein split products from the baby and placenta.

The sooner we get those facts in mind and apply them clinically, the more lives will be saved. We have had at the Research Hospital in the last ten years about 750 patients whom we classify as toxemias. We have lost only three. None of them had convulsions.

DR. BARKER (in closing).—Dr. Falls brings out the important point that in following these people, the more critically we have studied them the more we are impressed by the variability of toxemia of pregnancy. Our part in this program has been merely the attempt to bring out certain simple diagnostic points that might be used to differentiate some of those patients who are edematous who might be benefited by a high protein diet as contrasted to those who look the same, but are greatly endangered by taking any protein. If we can do that much, such an approach is exceedingly worth while. I think that a good, critical study of these people will bring out a lot more information which is obviously only beginning.

Hartman, C. G.: Facts and Fallacies of the Safe Period, *J. Contraception* 2: 51, 1937.

The writer summarizes the present status of scientific facts on the fertile period in women by asking the question: "Would you risk a patient's life by recommending her reliance upon the Ogino-Knaus schedule?" This is the crucial test. Emphatically not! For first, there exist effective contraceptive methods, almost 100 per cent effective in intelligent hands; second, there is still an element of doubt as to the variations in the time of ovulation in different women and fluctuations in the same woman, particularly since it is well known that the menstrual cycles may change in response to emotional upsets. Studies in the next few years will possibly reveal how safe the safe period is.

J. P. GREENHILL,

The ovary was enlarged and almost completely replaced by a cyst measuring 5.6 by 7.2 cm. The cyst was filled with clear yellow fluid. The inner surface of the cyst was in general smooth and glistening. At one pole a disk-like structure measuring 2.9 cm. in greatest diameter extended into the cyst. The external surface of this nodule was smooth and glistening and on section revealed a golden yellow cut surface. A small amount of apparently normal ovarian tissue was recognizable at the opposite end of the cyst.



Fig. 2.—Case 2. Islet of suprarenal cells in the ovary. Hematoxylin-eosin preparation, $\times 200$.

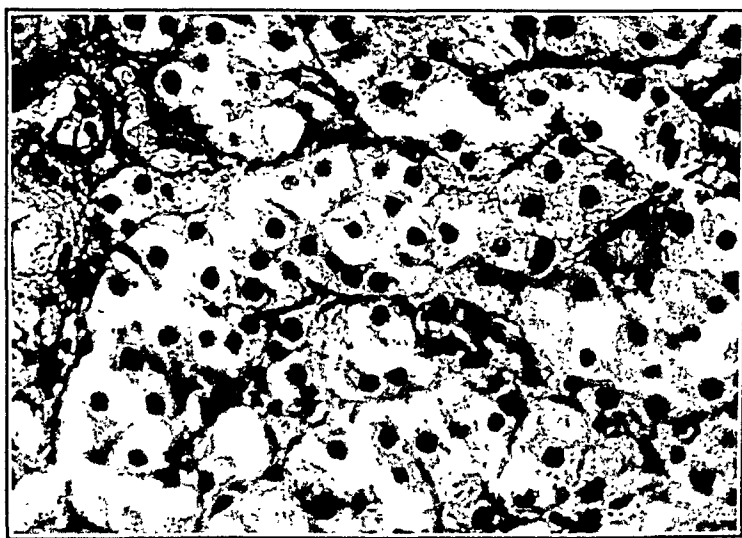


Fig. 3.—Case 2. High magnification of Fig. 2. Hematoxylin-eosin preparation, $\times 300$.

This tumorlike nodule of the ovary was found on histologic examination to be a large corpus luteum. In one corner, however, there were accumulations of very lightly stained cells. These were definitely smaller than the cells making up the corpus luteum and had eccentrically situated vesicular nuclei. Some of these cells showed an empty cytoplasm, while in others the cytoplasm was light pink. These cells showed no particular arrangement. Some were arranged in groups and rows which were separated from each other by small connective tissue fibers not containing any nuclear elements. There were no variations in the size, shape or staining

On the other hand it might well be possible that both types of tumor may exist or develop in the ovary, i.e., a hypernephroid tumor and a lutein cell tumor, both of which can and do give rise to interrenalism.

The following three reports are linked with this question of suprarenal-ovarian relation, either in the form of true tumor formation or of simple misplaced suprarenal tissue within the ovary. For reasons beyond our control endocrine studies could not be made.

CASE 1.—The first instance involves an ovary of a stillborn infant which was born at the thirty-second week of gestation. The gross appearance of the ovary was normal. Histologic examination showed a well circumscribed and apparently nodular area within the ovarian cortex but close to the surface of the ovary. This area consisted of an accumulation of large cells with foamy or clear cytoplasm and eccentrically situated vesicular nuclei. These cells showed no definite arrangement except occasionally when they seem to be in small rows separated one from the other by blood capillaries. Sections stained with sudan III showed the presence of fat within the cytoplasm of these cells.

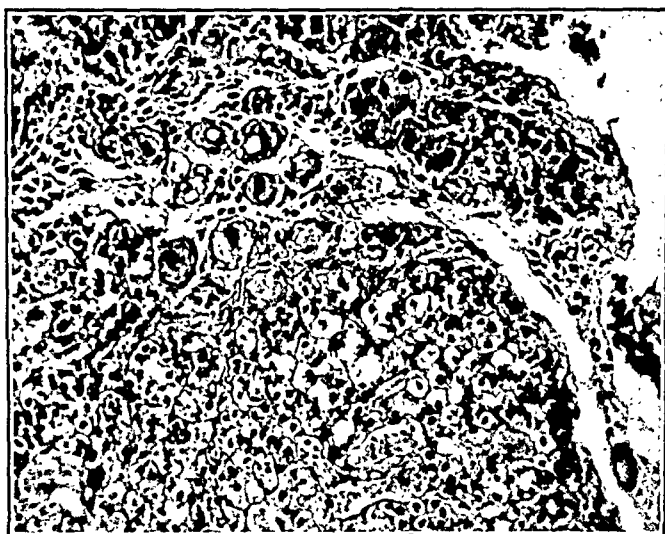


Fig. 1.—Case 1. Suprarenal tissue in the ovary. The upper part of the picture reveals infantile ovarian tissue, while the lower part shows the large cells with colorless cytoplasm. Hematoxylin-eosin preparation, $\times 90$.

This nodule corresponds to those described by Reichelt⁸ and by Neumann⁹ as misplaced suprarenal cortical tissue within the ovary. The unusual feature in this instance is the fact that the suprarenal rest was found in the cortex of the ovary rather than in the region of the ovarian hilus, which is the usual location.

CASE 2.—Mrs. M. B., aged 32 years, married, complained of sterility. Her previous history was as follows: She had had a spontaneous miscarriage at eight weeks in 1927. In 1928, she carried a pregnancy to term and was delivered by cesarean section for failure of engagement after twenty-eight hours of labor. In 1929 she suffered from an acute hyperthyroidism which responded to rest and medical treatment. In 1931, a second full-term pregnancy was terminated by an elective cesarean section in spite of the fact that the fetus was known to be an anencephalic monster. From 1931 to 1934, the patient suffered from hypothyroidism and menorrhagia which could be kept under control by the administration of comparatively large doses of thyroid extract. During this time and until the time of the ovariectomy in 1935, the patient was relatively sterile. In 1934, an appendectomy was performed for acute suppurative appendicitis. Six months later, routine pelvic examination showed no abnormalities. Four months later, April, 1935, the patient was again examined and this time an ovarian tumor, 6 or 7 cm. in diameter was felt. This was removed by laparotomy.

amenorrhea, and the change in pitch in the voice of the patient occurred at the same time. Removal of the growing tumor resulted in the re-establishment of normal menstrual habits plus a return of the voice to its normal pitch. This would seem more in favor of interrenalism resulting from the growth of suprarenal cortical tissue in the ovary.



Fig. 4.—Case 3. Ovarian tumor. Note the large cells with white (colorless, lipid containing) cytoplasm. Hematoxylin-eosin preparation, $\times 75$.

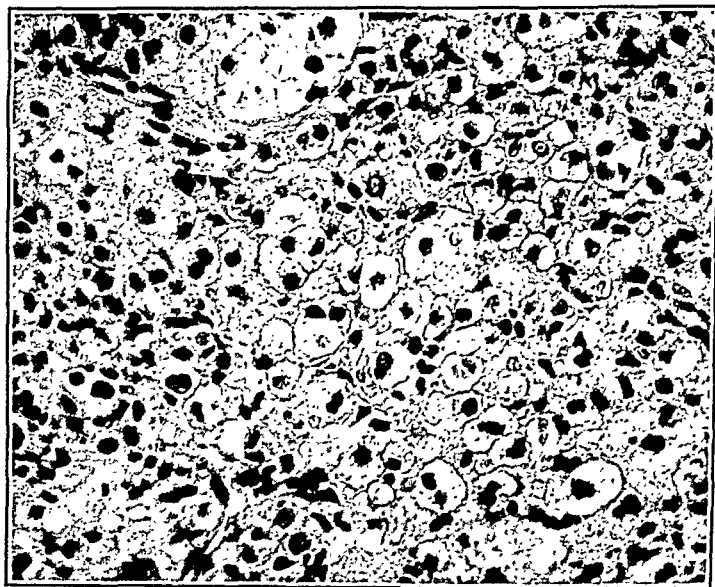


Fig. 5.—Case 3. High magnification of Fig. 4. Hematoxylin-eosin preparation, $\times 275$.

These three instances are quite similar in some respects. The ovaries in all three reveal accumulations of cells which morphologically resemble both lutein cells and suprarenal cortical cells. In the first two instances these cells were found in groups not actually representing a tumor growth; in the last case a definite tumor was found. None of the morphologic staining methods applied could serve as a definite differential diagnostic feature, and, therefore, on morphologic grounds

qualities nor were there any mitotic figures encountered. A sudan III stain revealed the presence of fat within the cytoplasm of these cells.

This accumulation of cells in the ovary which were found in the projection described above is difficult to explain. Though they differ morphologically from the corpus luteum cells, it is possible that these cells are lutein cells; but it seems more probable that they represent a suprarenal cortical rest in the ovary. The absence of any evidence of hemorrhage and blood pigment granules together with the absence of any form of reticulum speak for the suprarenal rest origin of this lesion. The sections of the ovary seem similar to those described by Saphir and Parker.¹⁰

After the histologic sections were examined, the patient was studied for evidence of interrenalism. It was found that she has a deep masculine type of voice which has been present since puberty. This type of voice may be correlated with the ovarian findings even though the voice has not changed in pitch since the tumor was removed (two years). However, it is of interest that she promptly achieved a pregnancy following the ovariectomy, and was delivered of a full-term, normal infant by cesarean section. Inspection of the pelvic viscera at this time revealed no abnormalities.

CASE 3.—(Courtesy of Dr. Wm. H. Rubovits, Attending Gynecologist, Michael Reese Hospital.) Miss F. Z., single, white, complained of amenorrhea of several months' duration and of a gradual deepening of her voice. Menses began at eleven years, were of the twenty-one-day type and always normal, with a five-day flow. During the menses three to four pads were used daily until two years ago. At that time there was daily spotting for four months, which required two pads daily. For the next six months, menses occurred every two weeks and lasted six days. During this period her voice, which had been of the high soprano type, gradually deepened to a very low contralto. She also experienced periods of extreme "nervousness" and attacks of palpitation during this time. Following this, the menses stopped completely, there being no vaginal bleeding for the seven months preceding operation. During all this time, her weight remained stationary.

Examination at the beginning of the period of amenorrhea revealed normal genitalia. Three months later the uterus seemed smaller than normal and definitely smaller than before. The left ovary was the size of a walnut and seemed to be solid in consistency. Re-examination five weeks later showed that this ovary had grown markedly and was about 6 cm. in greatest diameter.

A laparotomy was performed, and the enlarged left ovary was removed. The uterus and right ovary appeared normal but small. Menses were re-established six months later and have been of the twenty-six- to twenty-eight-day type, of four- or five-day duration and of normal quantity up to the present time. Her voice has returned to a high soprano pitch as it had been during the time preceding her menstrual irregularity. She has since married but has not become pregnant.

The ovary was ellipitical, measuring 5.5 by 4.0 by 3.5 cm. and weighing 40 gm. It was of soft consistency. The external surface was white and fibrous with soft nodular projections. On section almost the whole ovary was replaced by a soft reddish-yellow tumor. At one pole there was a rather well circumscribed yellow-red area which had a dark red center. Yellow dots were diffusely scattered over the surfaces. There were several red and pink fleshy areas.

Microscopic examination of the tumor revealed a new formation of cells showing a lightly stained cytoplasm and eccentrically situated and distinctly vesicular nuclei. In some portions, the cellular outlines were clear but in others, they could not be made out. The nuclei varied in size and shape. In many areas the cells resembled those seen in the corpus luteum, while in other areas they resembled suprarenal cortical cells. Mitotic figures were seen very occasionally. There were many areas of necrosis, marked degenerative changes and hemorrhages. The tumor was richly vascularized. In many fields the tumor cells surrounded the blood vessels, giving rise to peculiar perithelioma-like structures. Sections stained with sudan III revealed much fat within the cytoplasm of the tumor cells.

Here again, as in Case 2, it is possible that these cells are corpus luteum cells. In this case, however, it is more probable that they represent suprarenal cortical rests which had become neoplastic in character. The development of the tumor, the

I have in mind two cases in illustration: (1) A girl of 14, who had a few irregular menstrual periods, showed a hairy growth on the face, and on the body, and scant breast development. There was no hip development and she had a deep voice. She was very athletic and played with boys almost entirely. Rectal examination was not satisfactory. A pelvic pneumoperitoneum showed both ovaries to be cystic. A year later I performed a wedge-resection of both ovaries. I could not differentiate grossly or microscopically between this tissue and that of the common polycystic ovaries. In the two years following this operation the girl has developed feminine characteristics. Her breasts have enlarged, the menstrual periods have become regular, and the hips and knees have become rounded. The hairy areas over the sternum have not grown, the face hair is distinctly finer, a feminine type of escutcheon has appeared and the voice is more feminine.

(2) The second case was that of a woman of 43 years, married for sixteen years, who came to me having had periods of amenorrhea lasting for two months to about a year. She had a masculine build and a profuse coarse black beard which required daily shaving. The hair on her breasts and abdomen was of the masculine type, and she had a thick, firm panniculus and tough skin. She had never conceived before during her sixteen years of marital life, but the last amenorrhea was that of a pregnancy. At eight months she was delivered of a four and a half pound baby. She is lactating, which is quite surprising in this type of woman, her breasts having developed only late during pregnancy. I shall be very much interested in following her to see if there is a masculinizing tumor of the ovary.

DR. FRED H. FALLS.—There is one possibility of differentiating these tumors which may work out. We have recently taken blood from the human ovarian vein coming from an ovary with an active corpus luteum and were able to demonstrate its progestin action on the human uterus. Dr. Reis might have taken up blood from the ovarian vein on the side of the tumor, as it might have shown progestin. These are very rare tumors and anything that will help in the differential diagnosis is important.

FAMILIAL INTERSEXUALITY*

A REPORT OF THREE UNUSUAL CASES

DANIEL R. MISHELL, M.D., NEWARK, N. J.

THE subject of intersexuality, sex intergrades, and pseudohermaphroditism has long been a source of interest and investigation for the biologist. The essential nature of sex itself is involved in the question. The lower orders of animals and plants have furnished most of the basic knowledge of a phenomenon which for years has been the subject of contributions from medical writers who have described these deviations from the normal, as they occur in the human species.

No attempt is here made to present a comprehensive review of the contributions to the medical literature or of the fundamental work from the fields of experimental zoology and genetics. Reference is made, however, to the following reported cases in the literature since in various details they bear some resemblance to the cases about to be described.

*Read before the Association for the Study of Internal Secretions, Atlantic City, June 8, 1937.

it is not possible to differentiate beyond doubt between lutein cells and suprarenal cortical cells. The same, naturally, may be true of other similar case reports in the literature of both hypernephroma of the ovary and the lutein cell blastoma. At the present time it is well known that suprarenal cortical tumors (carcinomas) in young girls produce symptoms of virilism, pubertas precox, etc., whereas lutein cell tumors do not necessarily lead to interrenalism. In view of the clinical history of two of these cases, it seems likely to link the "interrenalism" with an excess of suprarenal cortical structures and, therefore, it would seem reasonable to designate these abnormal cell structures in the ovary as suprarenal cortical in origin.

SUMMARY

Three instances of apparent foreign cell structures in the ovary are reported. In the first, the ovary of a still-born infant revealed misplaced suprarenal cortical structures situated below the surface, opposite the hilus. In the second instance, such a structure was found in the wall of a cyst in an adult ovary. In the third, a tumor of the ovary, consisting of similar structures, was found definitely linked with the symptoms of interrenalism. The question of differential diagnosis between lutein cell tumor and hypernephroma of the ovary is discussed, and it is suggested that whereas on morphologic grounds a differential diagnosis is next to impossible, interrenalism is more likely to point toward the suprarenal cortical origin of the tumor cells.

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DISCUSSION

DR. OTTO SAPHIR.—Whereas histologic differentiation is extremely difficult, it may eventually be possible, by an examination of hormones, to differentiate between these two tumors. With the lutein cell tumors we may expect the corpus luteum hormone in the urine, but up to the present it is very difficult to detect traces of such a hormone. In instances of misplaced suprarenal cortical structures in the ovary, we might expect to find an increased amount of estrin in the urine. The history also is very important because where masculinization is very pronounced, it is more likely that the tumor arises from suprarenal cortical structures rather than from lutein cells.

DR. IRVING STEIN.—I have seen many patients who show marked masculinizing effects and in only a few are we able to demonstrate any lesion to account for it. We may be unable to determine existent lesions in the adrenals or ovary or possibly a microscopic area in some other endocrine gland. There are women who show distinct virilism shortly after puberty, others late in life.

Another sister, aged 30, showed a marked abnormality of fat distribution, indicating a pituitary disturbance, and for the past two years she has noticed a hypomenorrhea accompanied by vasomotor disturbances.

Examination of another sister, aged 37, revealed the presence of a fibromyoma. The remaining two sisters were apparently normal.

CASE 1.—M. D., aged 35 years, single, presented herself in December, 1935, complaining of a swelling in each groin. The past history was unimportant except for the fact that she had never menstruated. Since the age of 7, the patient noticed a

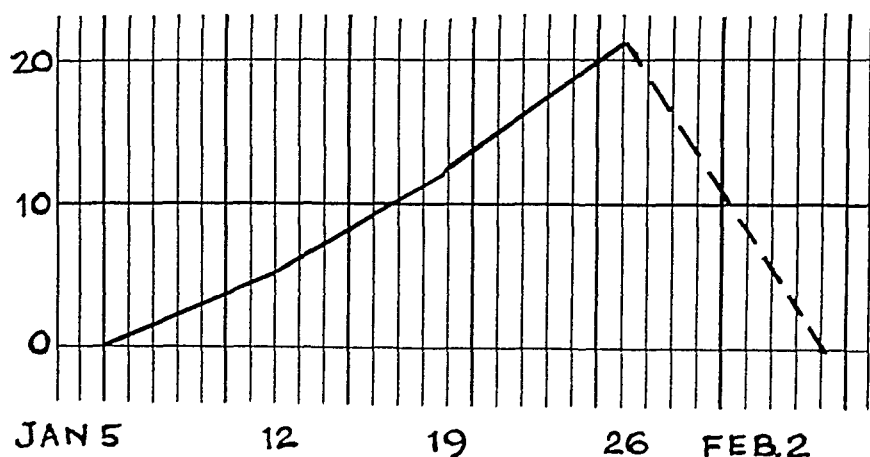


Fig. 1.—Estrogenic curve before operation (Case 1). Rat units in twenty-four-hour volume of urine.

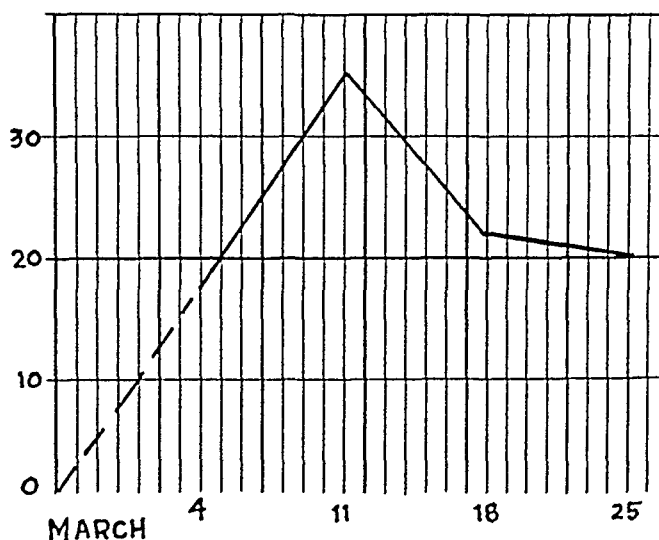


Fig. 2.—Estrogenic curve, postoperatively (Case 1). Rat units in twenty-four-hour volume of urine.

small lump in each groin about the size of a marble. These lumps gradually increased in size, more rapidly during the past five years. Three years ago she experienced pain in the groins especially upon exertion. There were no headaches, vertigo, or fatigability. She developed as a normal girl, was decidedly feminine in her traits and characteristics, and although attracted to men has never married.

Examination.—The patient was superlatively feminine in appearance and reaction. She had abundant cephalic hair, a clear complexion, free from hirsutism, and

In 1922, M. A. Goldberger¹ reported a case of pseudohermaphroditism in a "girl" of 14 years in whom a familial factor was suggested by two paternal aunts who had never menstruated and had exhibited no mammary development. Montgomery² in 1928 reported a case of androgynepseudohermaphroditism in a girl of 12 years, who had the general external appearance of a female and at operation was found to have testicles but no ovaries, tubes, or uterus. In 1930, Pryor and Brooks³ reported two cases of intersexuality. Other cases were reported by J. F. Hagerty⁴ in 1931; by P. C. Tung⁵ in 1932, who described a case of pseudohermaphroditism in a patient with the habitus of a male and a history of ejaculation of semen, but in whom a rudimentary uterus was found with gonads suggesting that they were ovaries; and by Hugh Young⁶ who, in 1933, described 14 cases exhibiting practically every type of pseudohermaphroditism. In 1935, Emil Novak⁷ reported a case and gave a general epitome of the mechanism underlying these anomalous deviations from normal dimorphism.

A comparison of the actual facts and case histories reported by the authors referred to discloses a somewhat indefinite nomenclature. Lack of precision in terminology is perhaps unavoidable at the present time; a situation well described by Professor Witschi⁸ who says:

Originally the terms hermaphroditism, intersexuality, and sex intergrades have been used to designate deviations in typically gonochoristic forms especially in man. It is futile to attempt to use these terms discriminately for different types of mixtures of sex characteristics both because each in the past has had such different connotations and because the combinations of sex characters appear so varied in morphologic and functional respects, in ontogenetic history and origin that every classification is annihilated by numbers of interclasses.

In the following report a detailed description of facts will be presented. Recently three sisters complaining of primary amenorrhea were carefully studied, and the findings encountered were so unusual from the standpoint of endocrinology and heredity that a description of these cases was deemed worthy of publication. The family history is important and is given in detail.

There were twelve children, nine of whom are living, between the ages of 23 and 37 years, eight females and one male, three having died in infancy. The mother is 62 years of age, in good health except for diabetes which was first noticed at the age of 49. The father died at the age of 67 following a prostatectomy. The mother's menstruation began at the age of 12, was regular at monthly intervals, and the menopause occurred at the age of 45. The mother has two half-sisters; one is 60 years of age and has *never menstruated*. A physician examined her many years ago and told her that her uterus was absent. The other half-sister is normal, married, and the mother of six children.

Routine examination of the five sisters, other than the three to be reported in detail, disclosed several endocrine defects. Of the five, only one, aged 28, had married and she gave evidence of sterility. Her external genitalia, vagina, and uterus were distinctly infantile in type. There was little pubic hair. The labia majora were small and underdeveloped, the vagina shallow, and the uterus measured only 2 inches by sound. Estrogenic studies of the urine showed a comparatively low hormone excretion.

palpated but no uterus, tubes, or ovaries were felt. The testis with the epididymis and part of the vas deferens was removed and the hernia repaired. A left inguinal incision was made; a similar condition was encountered and the same procedure followed.

Photographs were taken at the time of operation. Further examination while the patient was still anesthetized disclosed the presence of a vagina about three inches long, which ended in a blind pouch.

Subsequent to the operation the patient had enjoyed good health and has resumed her regular occupation. She had no symptoms of menopause until January, 1937 when she noticed the onset of occasional hot flashes.

An abstract of the report of the pathologic examination made by Dr. Edward Fendrick follows:

Gross.—The specimen consists of two oval bodies, the convex portions of which are covered with a shiny dense tunic except on one lateral margin where there appears to be an excess of tissue. On cutting both organs longitudinally the surface is seen to be reddish brown in color and extremely soft in consistency. Radiating fibrous tissue septa are seen to demark the origin from above downward. Close to the hilum of the organs the fibrous tissue septa become more prominent and appear characteristically like the mediastinum of the testicle.

Microscopic.—Sections from the testes give an appearance quite in accord with the normal histologic structure of the organ. The tunica albuginea is dense and well formed. Many of the secretory tubules show widening of the fibrous basement membrane with an appearance suggestive of hyaline changes. The microscopic appearance of the tissue removed from the poles of the epididymis shows a convoluted efferent duct lined with stratified columnar cells, the surfaces of which show numerous cilia. No spermatozoa can be found with these ducts."

In March, 1936, quantitative estrogenic studies were made upon four different specimens of urine and an appreciable amount of hormone was found as shown in Fig. 2. A prolan determination was made on May 28, 1936, which showed 400 M.U. per liter, a typical castrate amount. A photograph taken of the patient three months after the operation is shown in Fig. 3.

Subsequent examinations of the urine for estrogenic substance were made at various intervals from May, 1936, to March, 1937. Practically no hormone was found, the last report being 5 R.U. in twenty-four hours.

CASE 2.—P. D., a sister of M. D., aged 23 years. History disclosed that she had never menstruated. She had had no serious illness or operation. For the past three years she had been suffering from severe headaches, especially in the posterior occipital region. She complained of a dull aching pain in the right lower quadrant for the past year. A swelling, present in each groin since childhood, had increased in size during the past two years. These masses were prominent after the patient had been on her feet all day, and disappeared when she assumed a recumbent position.

Examination.—Height 69 inches, upper and lower measurements, 33 and 36 inches, respectively. Her general appearance was distinctly feminine. There was abundant growth of cephalic hair, complexion clear, and skin soft textured. There was no facial hirsutism and no axillary hair was present. The fingers were long and tapering. The teeth were normal in size, spacing, and position. There was no thyroid enlargement. Abdominal examination disclosed the presence of a right inguinal hernia the size of a small orange. Within the hernial sac could be felt a firm oval mass the size of a large olive, surmounted by a hard convoluted structure, tender to deep pressure. On the left side no hernia could be felt, but a similar ovoid mass, slightly larger than the right, was situated in the groin just beneath the skin.

a high-pitched, well-modulated feminine voice. The teeth were normal in size, shape, and spacing. The breasts were well developed but the nipples flat. Skeletal structure and growth was normal: height, 67 inches; weight 125 pounds; upper and lower measurements 32 and 35 inches, respectively; span 69 inches. The hands and fingers were normal in size. No axillary hair was present. Abdominal examination disclosed the presence of bilateral inguinal herniae, the right the size of a small orange, the left the size of a hen's egg. Palpation of each hernial sac revealed a freely movable, olive-shaped body, tender to deep pressure, on the superior pole of which was encountered a rather hard convoluted mass. The ex-

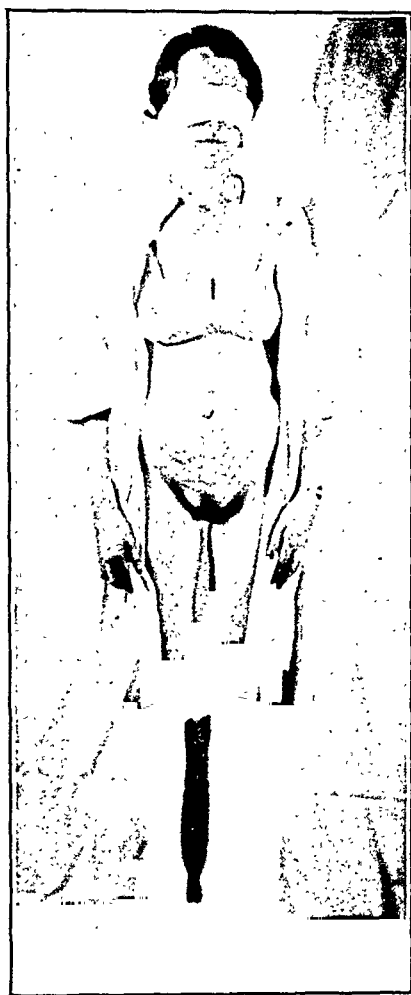


Fig. 3.—Photograph of patient three months after operation (Case 1).

ternal genitalia appeared normal. The pubic hair was sparse but feminine in distribution. The clitoris was small. The labia majora and minora were well outlined.

Laboratory examination showed a negative blood Wassermann and a basal metabolism of -14 . Quantitative estrogenic studies of the urine at four weekly intervals showed a definite amount of estrone as represented by the diagram (Fig. 1).

Operation.—Feb. 21, 1936. A right inguinal incision was made exposing the sac. Upon opening the sac an organ resembling a male gonad was found. This was attached to the sac at the lower pole by fibrous tissue resembling a gubernaculum testis and surmounted by a cordlike structure, a half centimeter thick, which looked like epididymis. The peritoneal opening was enlarged and the cord was observed to pass retroperitoneally downward and forward. The pelvic cavity was thoroughly

the phase of the spermatogenes. No spermatozoa or remnants of spermatozoa are found anywhere in testicle, epididymis or in any of the cystic formations. Ade-



Fig. 5.—Photomicrograph (Case 2) of section showing spermatic tubules and interstitial tissue.



Fig. 6.—Photomicrograph (Case 2) of section taken through epididymis showing ducts surrounded by fibrous tissue.

noma-like structures of different sizes, as often found in retained testicles, are present; one of them measures 3 by 2 by 1.3 mm. There are many partly calcific, partly noncalcific concretions around some of which the epithelial cells are arranged

Laboratory Findings.—Quantitative studies of the urine at four weekly intervals showed the presence of estrogenic substance as shown by the diagram (Fig. 4). No prolan was found in a specimen examined in May, 1936. A test for male hormone was made in June, 1936, at the Biological Laboratory of the Newark Beth Israel Hospital and showed the presence of 4 capon units per liter.

X-ray studies of the sella turcica and pelvis were made in June, 1936, showing a normal sized sella turcica and a typical female pelvis.

Operation.—June 29, 1936. A Pfannenstiel type of incision was made and the abdomen opened. A thorough exploration failed to reveal the presence of a uterus, tubes, or ovaries. An appendectomy was performed. After the peritoneum and fascia were closed the groins were explored. Organs similar in every respect to those found in Case 1 were found, and a bilateral orchidectomy was performed. The postoperative course was uneventful and the patient was discharged in good health on the twelfth day. An interesting feature was the disappearance of headaches following the operation. Specimens removed in this case were examined by Dr. Alfred Plaut, Pathologist to the New York Beth Israel Hospital, who submitted the following report:

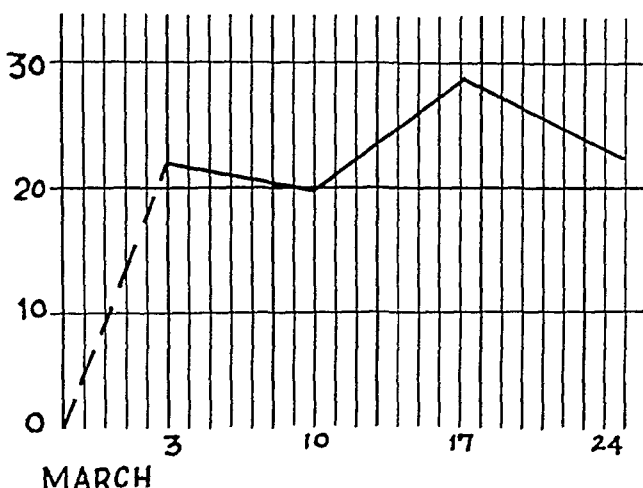


Fig. 4.—Estrogenic curve, preoperatively (Case 2). Rat units in twenty-four-hour volume of urine.

Gross Specimen.—Two testicles with coverings, epididymis, and spermatic cord. The left measures 4 by 2.5 by 1.2 cm. The spermatic cord can be palpated for about 7 cm. The right testicle measures 4 by 2 by 1 cm.; the cordlike structure is about 6 cm. long. From outside both testicles, which are normal in size, show nothing unusual. There are adhesions and few small hydatid-like formations.

“The cut surfaces, after a few hours fixation, appear brownish throughout with a few small gray strands irregularly radiating from the region of the rete. Near the middle of the cut surface of the right testicle two small soft, yellowish gray structures, about the size of a small rice grain, protrude. No attempt is made to pull out tubules from the cut surface. According to this picture, we do not deal with any gross abnormality of testicle, epididymis, and proximal portion of cord.

“Since no trace of female gonad had been found at operation, we wanted to make sure that even the slightest admixture of another structure to the testicular tissue would not be overlooked. The testicles, therefore, were examined in serial sections. After this examination it seems almost impossible that any structure should have escaped attention.

Microscopic Examination.—The slides give the characteristic picture of retained testicle (Figs. 5 and 6). The tubular epithelium is not developed beyond

others a fine cytoplasmatic network extends from the nucleus to the periphery of the cell. (Probably much of this variety is due to irregular shrinking.) Some of the cells deserve the name of spermatogonial giant cells. Cells between 20 and 30 micra are frequent, some reach 44 micra. Occasionally smaller cells with indefinite brown pigment-like granules are seen. The Sertoli cells appear pressed against each other, their nuclei are long and situated in the axis of the cell. There are some cells with two nuclei (probably not Sertoli cells). On the whole, the epithelium, like any other single factor in this testicle, shows nothing essentially different from the corresponding structures in other retained testicles.

"Any, even trifling, seeming irregularity in the histologic picture was studied carefully in the attempts at finding something unusual in the testicle. As mentioned before, nothing has been found that would set apart this testicle from any other retained testicle.

"In summing up, we see the characteristic picture of retained testicle: fibrosis, lack of spermatopoiesis, adenoma-like formation, calcific bodies, lack of pigment in the epididymis. In spite of all efforts, no unusual histologic feature can be detected."

Estrogenic studies of the urine made subsequent to the operation showed an appreciable amount of hormone up to August, 1936, when 37 R.U. in twenty-four hours were found. Later determinations revealed practically no estrogenic hormone but did show the presence of gonadotropic substance. These latter determinations were made in the laboratory of Dr. R. Kurzrok at the Medical Center, Columbia University, New York City.

CASE 3.—A. D., sister of M. D., aged 32 years. History disclosed the fact that she had never menstruated. Hair had turned prematurely gray at the age of nine years. There were no headaches, vertigo, or palpitation. She was not easily fatigued or nervous. General health good. Weight at the time of examination was 139 pounds, height 67 inches, upper and lower measurements were 33 and 34 inches, respectively. General appearance was distinctly feminine. She was intelligent, cooperative, and emotionally stable. Well-modulated feminine voice; cephalic hair abundant, soft in texture and gray in color. Skin soft, no hirsutism. Teeth close together and normal in size and shape. Hands and fingers normal. No tremor or goiter. Breasts moderate in size and shape, nipples normal. Pubic hair, feminine in distribution. Palpation of the abdomen revealed a mass present in each groin, the size of a pigeon's egg. The masses were sessile, freely movable and slightly tender to deep pressure. There was a hard, irregular mass surmounting the upper pole, suggestive of an epididymis. Rectal examination failed to reveal the presence of a uterus. The basal metabolic rate was -12. Quantitative estrogenic studies of four weekly specimens of urine showed a curve similar to those of the two previous cases. No further study was made in this case.

The cases here presented are unusual for at least two reasons. *First*, there is a well-established familial history involving three sisters and a maternal aunt. In the case of two of the sisters, the data relating to the gonads have been verified by operation and histologic examination, and by hormonal assay. *Second*, these cases present not the rather commonly found combination of mixed secondary sexual characteristics and primary sex tissue found in the usual pseudohermaphrodite, but a condition in which there is a typical male gonad, and so far as could be ascertained, male gonad alone, associated with well-developed secondary

in radiating fashion. There is moderate 'fibrosis testis.' This means that the walls of the tubules are hyalinized. There is, however, no increase of fibrous tissue between the tubules.

"The interstitial cells are much more numerous than in the normal testicle. This increase of interstitial tissue is real beyond any doubt. This must be emphasized because some authors are inclined to doubt the actual increase of interstitial cells and attribute the apparent increase to the atrophy of the testicle. In our case the pictures are convincing without any special investigation. Rather large masses of interstitial cells are also found in the epididymis and in the spermatic cord, at points where in control testicles only occasional very small groups of such cells are seen. The topographic relation of interstitial cells to nerves is very striking. There are, in the testicle, very large heaps of interstitial cells with much variety in cellular character, size of cells, staining characteristics, content in the larger heaps. The conclusion seems permissible from the serial sections that many of the larger heaps of interstitial cells are undergoing fibrous change. No search for crystals is made. Small round homogeneous droplets surrounded by interstitial cells probably represent a product of the cells.

"The largest more diffuse masses of interstitial cells are located near the poles of the testicle. The interstitial cells are growing around the tubules and seem to choke them. There are some giant interstitial cells (60 by 30 micra, nucleus 10 micra diameter, nucleolus 4 micra diameter; in another cell the nucleus measures 24 by 16 micra). In places almost all the connective tissue cells seem to be undergoing the change to interstitial cells. The two small nodules seen with the naked eye obviously correspond to large heaps of interstitial cells. There are no marked blood vessel alterations.

"Solid epithelial nodules and glandlike formations are present in the outer lining of the albuginea. Since the textbooks do not mention such formations in the normal testicle, the possibility has to be considered that we might be dealing here with something characteristic of the testicle in an otherwise female body. This supposition has something plausible about it because the peritoneal epithelium in the female pelvis has a great tendency toward the formation of such structures, notably on the tube and the broad ligament. Examination of a number of testicles, however, revealed that such formations may be found in otherwise normal testicles from male individuals, even in the parietal layer of the tunica vaginalis. Furthermore, in our case many epithelial and glandular structures are seen at different points in the albuginea. On studying the series it becomes clear that they are continuous with the rete. This also applies to narrow glandular ducts which in the single section seem to be far away from the rete.

"Attempts are made to differentiate several layers in the albuginea because at different ages these layers behave differently. No characteristic arrangement of the layers in the albuginea can be seen. As controls, slides from many different testicles are stained with the von Gieson mixture and with Weigert's elastic tissue stain. There is nothing remarkable about the rete testis.

"The epididymis also conforms to the picture generally encountered in the retained organ, so far as its epithelium is devoid of pigment. No cystoid changes are seen. The musculature in the epididymis at some points appears rather thick.

"*The Epithelium in the Tubules of the Testicle.*—Needless to repeat, no spermatozoa are seen in any of the sections, neither in the epididymis nor in the testis proper. The epithelial cells nowhere are developed beyond the spermatogonial phase. The cells vary considerably in size and structure and the same applies to the Sertoli cells which are numerous. Large cells with vesicular protoplasm and with empty spaces between the nucleus and the outline of the cell are conspicuous. In some the nucleus is surrounded by a thin layer of intensely staining protoplasm, in

Several months after operation the hormone disappeared from the urine and gonadotropic substance was found to be present. We may assume, therefore, that the testes produced the female sex hormone in these cases and following operation the pituitary gland, uninhibited by the gonads, produced that amount of gonadotropic substance usually found in castrates and in menopausal states.

I wish to express my appreciation to Drs. Raphael Kurzrok, Alfred S. Plant, and Edward Fendrick for their helpful suggestions and aid in the study of these cases.

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MEDICAL TOWER

DETERMINATION OF THE ESTROGENIC SUBSTANCE IN BLOOD SERUM BY MEANS OF AN ESTIMATION OF THE ANTIPROTEOLYTIC POWER OF THE SERUM

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IT IS an old observation that during pregnancy the female host develops properties antagonistic to the proteolytic or digestive activities of the parasitic fetus. Both Adami¹ and Blair-Bell² recognized the significance of the interaction between the invasive fetal cells and the protective powers of the maternal organism. Blair-Bell was interested in this problem on account of its bearing on the invasive ability of malignant cells, and the body's defense reaction to them. Grafenberg³ in 1909 pointed out that the decidua contained factors which were able to neutralize the proteolytic power of young placental villi. Abderhalden⁴ some years earlier had initiated the studies which were finally reported in 1912 in his publication, "Defensive Ferments of the Animal Organism." He described a test for pregnancy based upon the presence in the blood of the mother of ferments capable of digesting placental peptides. These agents could be demonstrated about eight days after impregnation, persisted throughout the whole pregnancy, and disappeared within fourteen to twenty-one days after the expulsion of the placenta. These "defensive ferments" were to be found even in the blood of the mare, in whom the villi are excluded from the maternal blood stream.

The author, suspecting that spontaneous abortion in man might be due to an increased maternal resistance to villous encroachment on the uterine muscle, which in turn would lead to an insecure foundation for the whole fetal structure, investigated the blood sera of a series of aborting women for antiproteolytic powers. On exposure to trypsin under standard conditions, they displayed antiproteolytic prop-

sex characteristics of the female, while the hormonal assays revealed a large amount of estrogenic substance.

The familial element in these cases would seem to suggest a defect in development arising in an abnormal variation of the influence of the genic factors *determining* sex and the environmental, extranuclear factors *controlling* sex development. If this is true these cases are remarkable in the extent to which the developmental controlling factors have overridden and completely suppressed the zygotic or genic sex determining factors.

The evidence today seems entirely adequate to support the generally accepted view that sex, at least in mammals, is genetically *determined* and depends upon the chromosomal pattern established at fertilization: the XX chromosomal type determining the female and the XY the male. In most cases the original sex-determining genic factors subsequently control the development and differentiation of the organism along the lines laid down in the genetic pattern. In such cases the primary sex tissue of one or the other sex (testis or ovary) as determined by the chromosomal type, elaborates the characteristic hormone whose subsequent action serves to differentiate the Müllerian or Wolffian ducts, and hence develops a typical male or female individual, since in all individuals, regardless of genetically or zygotically determined sex, the embryonic *anlage* is bisexual, i.e., there develop two pairs of gonaducts: the Wolffian ducts and the Müllerian ducts, the one potentially male and the other female. In other orders as well as mammals there is convincing evidence that even where sex is genetically determined, the sex differentiation of the opposite sex may take place. This seems to be a possible explanation of the cases here reported.

The final determination of whether the development and differentiation of one or the other sex potentialities as represented in the bisexual *anlage* shall proceed along the lines as genetically determined, or that of the opposite sex, seems to resolve itself into a question of the predominance of the two factors, the zygotic and hereditary, on the one hand, and the environmental or ontogenetic, on the other.

It is believed that the cases here reported present a unique instance of this dual developmental control in the human species.

CONCLUSION

A report has been given of three sisters, two of whom were operated upon and found to have male gonads with complete absence of ovaries, tubes, and uterus. The third sister presented these facts by clinical examination. All three showed the presence of estrogen in the urine before operation. The question arises as to the origin of the female sex hormone which was found in the urine and which was necessary to stimulate the development of the feminine secondary sex characteristics.

3. Add 0.5 c.c. of blood serum to 3.5 c.c. of buffer solution in each of two Wassermann tubes (100 × 11 mm.). Plug one with cotton wool and incubate it for thirty minutes at $55 \pm 5^\circ$ C.

4. Cool the heated tube and add to both it and its unheated mate 1.0 c.c. of a commercial trypsin solution in glycerin and water. This solution is made from a stock solution prepared by dissolving 1 gm. of trypsin (Digestive Ferments Co. of Detroit, U. S. A.) in 75 c.c. of glycerin and 25 c.c. of distilled water. This stock solution can be used for six months or more, as it will retain its potency in the refrigerator for that length of time. Just before the test is to be made, 0.2 c.c. of this stock solution is added to 100 c.c. of distilled water, making a 1/500 of 1 per cent solution of trypsin. It is this solution that is added to the serum-buffer mixtures after it has been brought to the same temperature as those mixtures.

5. Cork both tubes and incubate at 42° C. Sample each tube at intervals of ten minutes by withdrawing 0.5 c.c.

6. Add each such sample to 5 c.c. of distilled water containing five drops of phenolphthalein solution (50 mg. of phenolphthalein powder dissolved in 100 c.c. of a 50 per cent solution of ethyl alcohol).

7. Titrate the samples against fresh N/70 sodium hydroxide solution in a micro-burette.

8. The standard for these titrations is 10 c.c. of phosphate buffer (Kolthoff) at a pH of 9, containing 10 drops of the phenolphthalein solution just mentioned.

The end point is read without difficulty. If a lower pH than 9 is used for the end point the accuracy is decreased, but a slightly higher pH than 9 does not affect it.

No preliminary titration of the tubes before incubation is necessary. Readings are taken immediately upon sampling, until four or more such samplings have been titrated.

Those laboratories which have used this test have frequently had difficulty in setting up a normal control serum. Workers were astonished to find that the sera of many people presumed to be normal contained an excess of estrogenic substance. There are two ways in which such a difficulty may be obviated. Sera may be pooled and kept standing in the refrigerator for two weeks, by which time the estrogenic anti-proteolytic factor can no longer be detected by this test. Or, if the sera be kept at 70° C., the estrogenic material disappears much more quickly.

The alternative method of securing a "normal" serum is to use serum only from individuals saturated with a potent wheat germ oil. This scarcely answers the strict definition of a control serum, of course.

We have found it convenient to test three sera simultaneously, the one a control and the other two unknowns, under exactly parallel conditions. These are set up as follows:

TUBE 1 A (CONTROL)		TUBE 2 A		TUBE 3 A	
3.5 c.c. buffer solution		3.5 c.c. buffer solution		3.5 c.c. buffer solution	
0.5 c.c. normal serum		0.5 c.c. Serum 2		0.5 c.c. Serum 3	
1.0 c.c. trypsin solution		1.0 c.c. trypsin solution		1.0 c.c. trypsin solution	
TUBE 1 B (CONTROL)		TUBE 2 B		TUBE 3 B	
3.5 c.c. buffer solution		3.5 c.c. buffer solution		3.5 c.c. buffer solution	
0.5 c.c. normal serum		0.5 c.c. Serum 2		0.5 c.c. Serum 3	
1.0 c.c. trypsin solution		1.0 c.c. trypsin solution		1.0 c.c. trypsin solution	

CAUTIONS

1. The temperature given in this technique must be adhered to. An automatically controlled oven is perhaps the best method of maintaining the temperature of the tubes, and provides easy access to them for sampling. It has proved superior to the water bath.

erties not possessed by the blood sera of most women during pregnancy.⁵ This was found to be due to the presence in these blood sera of an excess of estrogenic substance,^{6, 7} which in turn was dependent upon deficiency of vitamin E⁸ in the body. The writer has postulated that estrogenic substance and vitamin E exist in the blood serum in equilibrium—and this seems to be true for nonpregnant human beings and some species of animals as well. No patient receiving an adequate or “saturating” dose of a potent preparation of vitamin E displayed in her serum the antiproteolytic properties associated with the presence in that serum of an excess of estrogenic substance. On the other hand, it was found that any normally digestible serum could be rendered antiproteolytic by the addition of estrin *in vitro* or by the administration of estrogenic substances to the patient before the blood sample was withdrawn. As has been said, the same sort of “E-estrin equilibrium” appeared to be demonstrable in rats, and the observation has been extended to both human and rat males since.

As the serologic test that has been developed is simple, can be quickly performed, and requires only a minimum of material and expense, it seems desirable to describe it again in detail, with the addition of one or two minor modifications of which subsequent experience has demonstrated the value. Up to the present, 2,493 such tests have been made on the blood sera of 1,204 men and women, 55 rats, 3 guinea pigs, and 3 rabbits.

The results appear to have clinical significance in the diagnosis and treatment of cases of a varied nature. Indeed, the importance of excess of estrogenic substance in the organism as an etiological factor in many different pathological conditions is just beginning to be recognized. The test has been significant in cases of abortion,⁵ miscarriage and premature labor,⁷ abruptio placentae,^{9, 10} (especially in helping to differentiate it from acute appendicitis and placenta previa), such menstrual difficulties as menorrhagia,¹¹ dysmenorrhea, amenorrhea, and the menopause. It enables one to differentiate between the mild toxemias of late pregnancy, and hence enables one to treat them on a more logical basis. Abortion, miscarriage, or abruptio placentae are predictable weeks or occasionally months before they develop in such form as to be clinically recognizable. It would seem, therefore, that the sera of all antenatal patients should be tested for the presence of excess of estrogenic substance in order to ensure proper prophylactic treatment if such a source of potential danger is revealed.

THE TECHNIQUE OF THE TEST

1. By means of venepuncture withdraw enough blood to give 1 c.c. of blood serum. Separate the serum promptly and keep it in corked tubes in the refrigerator until tested. Use no preservative. The test may be done as late as three to five days after the blood is withdrawn, but should if possible be done within the first twenty-four hours.

2. Make a fresh phosphate buffer solution (Kolthoff) from (a) 19.10 gm. of borax (B.P.) dissolved in 1 liter of distilled water, and (b) 13.61 gm. of sodium dihydrogen phosphate (B.P.) dissolved in 1 liter of distilled water. The solutions (a) and (b) should be combined in such proportions as will give a pH of 8.0.

be tardy in its onset, but carried on at the temperature and under the other standard conditions of the technique described it should always begin in a normal serum before the "forty minute reading" is taken. It then proceeds rapidly, soon reaches a peak of acid production, after which "reversal" occurs and progresses even more rapidly. This phenomenon of reversal indicated in the digest curves above seems to have eluded satisfactory explanation, but those who have studied trypsin

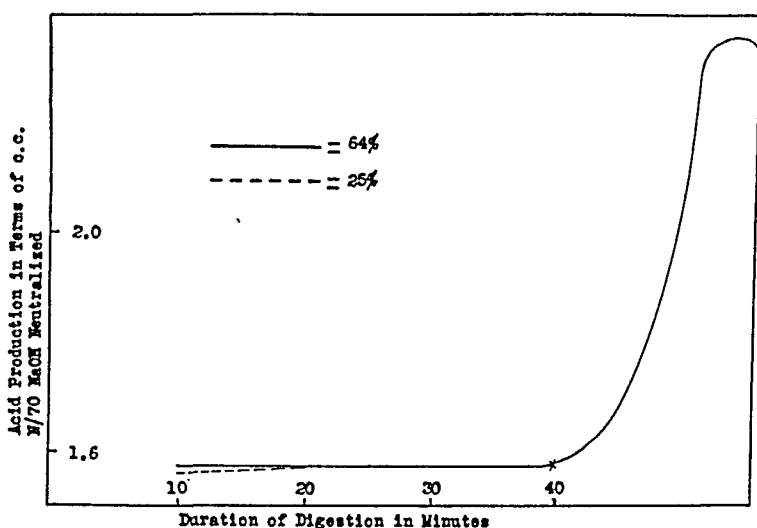


Fig. 1.

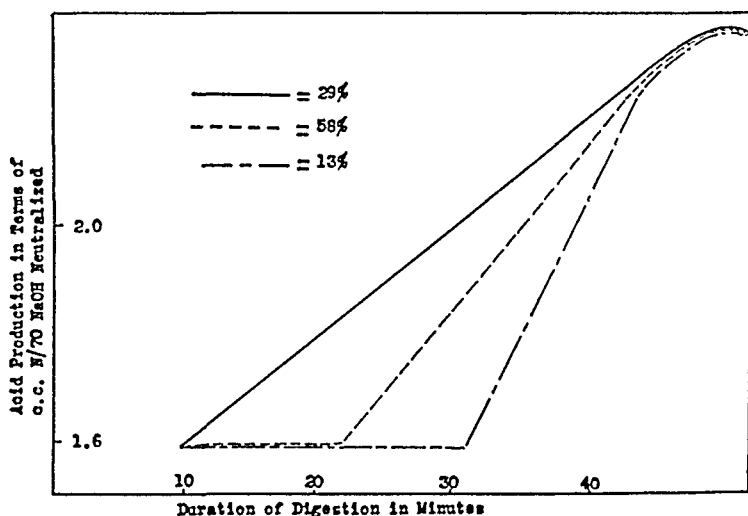


Fig. 2.

digests have consistently observed it. It occurs sooner when the digestion is carried on at higher temperatures and then, too, the total acidity present in the digest decreases more rapidly after the reversal, making the downward slope of the curve more steep. The reversal phenomenon may be a source of confusion to those using this technique for the first time, as in such digests as are described here the whole digestion which the dilute trypsin solution can effect may occur within twenty minutes after that digestion has once begun. The result is that

2. Whenever a tube is handled its contents should be mixed well to facilitate uniform digestion. The quickest and most thorough way by which to do this is to invert the corked tubes.

3. Each tube used must be strictly comparable to its fellows in both color of glass and dimensions and must not be washed in acid or alkali.

4. The trypsin stock solution is best prepared by first dissolving the trypsin powder in the water, then adding the glycerin required.

5. The standard tube at pH of 9 should be prepared afresh for each series of tests. It fades rapidly.

6. In comparing the large tubes during titration it is often found very difficult to tell exactly when one has come up to the end point, but it is a very easy matter to determine when one has gone just one drop too far. Therefore, always titrate to what seems to be the end point, then add drops one at a time until the end point is definitely passed.

7. Often the sera contain bile or hemolyzed blood or are turbid. These cannot be accurately matched against the standard. Accordingly it is customary to bring the tube containing the first sampling as close to the standard color as possible, then to dispense with any further use of the standard, and bring each succeeding sample to the exact color of the first sample. In this way contamination of the serum is no handicap in color matching.

8. The samples must be titrated by daylight.

OBSERVATIONS

In the normal sera, digestion might begin promptly in both the heated and unheated tubes, or be somewhat delayed in one or both. However, digestion always commenced before forty minutes had elapsed, when carried on under the conditions prescribed above for the process. It was under way in both tubes before twenty minutes in 29 per cent of the normal tests, before thirty minutes in 58 per cent, and by forty minutes in all. To illustrate the effect of the preliminary heating of one tube in each digesting pair, it may be mentioned that digestion began in both at exactly the same time in 45 per cent, but earlier in the heated than unheated tube in 60 per cent of the remainder. The preliminary heating of one tube of each pair is purely empirical. In 28 per cent of the cases tested, only the heated tube revealed anti-proteolysis or, in other words, revealed an increase of estrogenic content. This is the justification for the preliminary heating, indeed. Without it, the test would detect only three of every four cases whose sera contains an increase of estrogen.

In the sera showing abnormal resistance to proteolysis, digestion was sometimes found to begin in either one of a pair of tubes, when at the same time its mate revealed no evidence of tryptic digestion, or on the other hand both tubes of a pair might be equally resistant to digestion. Digestion was "inhibited" in only the unheated tube in 32 per cent of these resistant sera, in only the heated tube in 28 per cent, and in both tubes in the remaining 40 per cent.

There were several variant types in the digestion curves of these resistant sera (see Fig. 1). On the other hand, a normal serum, either in the heated or unheated tube revealed digestion curves as illustrated in Fig. 2.

The crux of the matter appears to be that the digestion of these serum-buffer mixtures by trypsin solution takes place according to the all-or-none principle. It either occurs or it does not occur. It may

allel resistance to the breakdown of simple proteins and simple carbohydrates. As was indicated above, Wunderly¹² using a nephelometric method, has independently found that certain human blood sera are resistant to proteolysis. His digestion curves as published display prolonged periods of inhibition of proteolytic digestion. These would probably be shortened if the digestion were carried on at higher temperatures, as I have found that the duration of effective resistance to proteolysis is shorter at 42° C. than at 37° C. (the temperature at which Wunderly worked) or lower temperatures.

A simple method for the determination of significant amounts of estrogenic substance in the blood has long been a desideratum. So tedious and expensive have previous methods been that urinary assay has been the method more widely used. That there is no necessary correlation between urine and blood estrin content has been demonstrated by many workers.¹⁷⁻²¹ The fallacy of conclusions based upon estimations of urinary estrogenic substance should be obvious, therefore. It is hoped that the method outlined here may point the way to a solution of this difficulty.

The values for estrogenic substance obtained by this method must appear very high to those who are familiar with the figures obtained for normal pregnant and normal nonpregnant women by Frank and his collaborators,¹⁷ Siebke²² and others. However, the Smiths by means of improved extraction methods have recently shown that Frank's figures for pregnant women are four to six times too low.¹⁹ Schlossberg and Durruty²³ were able to demonstrate that estrogenic substance in relatively large quantity was left in the residue after extractions of blood were made for the Frank assay. Their results are of great interest for comparison with the author's. For example, they extracted 1 rat unit per c.c. from the serum of several "normal" men and women, several women who had been castrated or were postmenopausal and even from the serum of several species of experimental animals. Therefore, it should not be very surprising if abnormal pregnancies, in which the amount of estrogenic substance in the blood is raised, should show an increase of two to three times above that quantity of estrin found in many such normal blood sera.

A similar and perhaps identical estrogenic substance to the one we have described,⁵ was reported prior to my publication by Engel of Vienna.²⁴ It was also water-soluble and acetone-soluble, gave positive estrin smears, but did not produce uterine enlargement in castrated mice. It also was highly unstable.

It was pointed out in a previous paper⁸ that there was an antagonism in the body between estrogenic substance and vitamin E. Probably the therapeutic effect of wheat germ oil depends upon that relationship. That such is the case is indicated by the wide variety of clinical cases other than those concerned with pregnancy in which the estrogenic substance has been found to be elevated and that such cases have in most instances yielded readily to treatment with wheat germ oil. As examples selected from my private practice, there may be listed

a reading taken after the end of that time may reveal a lower figure for the total acid present than was found at the beginning of digestion. A possible explanation of the "reversal" might be that it is due to the liberation of di-amino acids by peptidase action after the production of total acid has reached a maximum.

That in 25 per cent of the resistant sera the acidity reading at ten minutes may be slightly lower than the constant readings obtained consecutively at the twenty-, thirty-, and forty-minute intervals can be seen also in the somewhat analogous digestion curves obtained by Wunderly.¹² He, too, observed that there was a preliminary sharp rise of the total acidity in his digests, that this might continue to increase for a few minutes beyond the initial ten minutes of digestion, and that this rise preceded the period of inhibition of proteolytic digestion.

An effort was made to determine approximately the sensitivity of this antiproteolysis test for estrin. Normal pooled serum was allowed to stand in the refrigerator for at least twelve days, and other pooled serum was kept for twenty-four hours at 60° C., in order to allow as much as possible of the estrogenic substance present in it to deteriorate. A preliminary test of such sera revealed negative tests for estrogenic substance. Then varying amounts of aqueous theelin (standardized to 60 rat units per c.c.) were added to 1 c.c. samples of these blood sera and the resultant solution left to stand for three hours each. It was found consistently that any of these samples of normally digestible pooled serum could be made resistant to proteolytic digestion by adding 2½ rat units or more of this aqueous theelin to 1 c.c. of the serum. It is not certain whether only a fraction or all of the theelin added became involved in the inhibition of proteolysis, but the results were so constant as to lead to the suspicion that all of its active estrogenic component was involved in these rough tests.

DISCUSSION

At the same time as resistance to proteolysis in the blood serum of aborting women was reported by me, a somewhat similar phenomenon, namely, resistance to the fermentation by yeast of a monosaccharide added to certain pregnant women's blood serum, was reported in Germany by Eufinger and Sprado.¹³ They found that the quantities of this "inhibitor" in the blood corresponded to the blood estrin curve during and immediately after pregnancy. Moreover its value was low in cases of hyperemesis gravidarum and high in the late pregnancy toxemias, just as has been found for the antiproteolytic factor.^{14, 15} During the menstrual cycle it rose and ebbed similarly to estrin. However, Mommsen and Thyssen¹⁶ demonstrated that it was neither estrin nor anterior pituitary hormone that produced this antisaccharolytic phenomenon in blood sera. Moreover, this inhibition could not be demonstrated in sera after the menopause, nor in the blood of normal men. It is of considerable interest, however, that blood sera displayed, in certain physiologic and pathologic states, an approximately par-

VAGINAL HYSTERECTOMY*

A STUDY OF 348 CASES

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WHILE vaginal hysterectomy has not become widely popular in this country, nevertheless, it is enthusiastically praised by a small group of surgeons who have perfected themselves in the technique and have had an opportunity to observe the advantages of this procedure, when compared with hysterectomy performed through the abdominal route.

In the recent gynecologic literature, there appeared many excellent articles purporting to demonstrate the advantages of total abdominal hysterectomy over the subtotal operation.

E. H. Richardson¹ states that Von Graff collected nearly 1,200 cases of cancer of the cervical stump following subtotal hysterectomy. Two-thirds of these cases were reported within the last twelve years. It is quite probable that this does not represent the total incidence, since scattered cases must have been observed and not reported. Richardson further states that in a study just completed at the Johns Hopkins Hospital Clinic, and not yet published, Erle Henriksen found among 940 cases of cancer of the cervix an incidence of 2.3 per cent of stump cancer, and that in similar statistical reports the incidence of cervical stump cancer runs as high as 4.0 per cent. Fully two-thirds of the cases of stump cancer thus reported followed subtotal hysterectomy for fibroids.

The general belief that the coning out of mucous membrane of the cervical canal at the time of subtotal hysterectomy, or the destruction of it by cautery, as a prophylactic measure for subsequent development of stump cancer, is erroneous; this becomes evident when one recalls that more than 80 per cent of all cases of cancer of the cervix originate from the squamous cell epithelium of the portio vaginalis. Statistical studies show that of the large percentage of women who have had subtotal hysterectomies performed on account of the later consequences of uterine and tubal infection, about 20 per cent, who have never been pregnant, develop cervical stump cancer. This serves to focus our attention upon the possible rôle which chronic infections of the cervix play in the etiology of cancer.

In a recent paper J. R. Goodall² calls attention to the cause for the far greater incidence of postoperative complications in the subtotal over the total hysterectomy, and he enumerates them as phlebitis, pelvic cellulitis, embolism, peritonitis, and

*Read at a meeting of the Obstetrical Society of Philadelphia, December 1, 1936.

functional menorrhagia, and dysmenorrhea, and a type of vaginitis to be described in a forthcoming publication. Such cases, of course, prove nothing beyond the fact that wheat germ oil probably has a place in the therapy of conditions other than those connected with pregnancy. Its use would appear to be indicated when the blood estrogenic content is elevated above normal. Whether or not it will prove helpful in any such case can readily be determined within the first few days of its use.

Rowlands and Singer²⁵ have shown that in states of E-deficiency there is a decrease in the content of gonadotropic material in the anterior pituitary. However, the corpus luteum is not affected. This is not inconsistent with the hypothesis advanced previously⁸ by me, namely, that in vitamin E defective conditions there is an excess of estrogenic substance in the organism.

SUMMARY

1. A simple laboratory test for the presence of estrogenic substance in the blood serum of animals and man is described in detail. It requires 1 c.c. of blood serum and can be completed in about one and a half hours.

2. We have used it in 2,493 tests on 1,204 human beings and 61 experimental animals in the course of the last three years.

3. Its clinical significance is discussed, especially in view of the accumulation of estrogenic substance in the blood serum in cases of deficiency of vitamin E.

Thanks are due to Drs. Sharp and Laughton of Parke, Davis and Co., Detroit, Michigan, for ample supplies of theelin. The author is also grateful to Professor A. B. MacCallum and Mr. G. A. Adams for the opportunity of working in the Biochemical Laboratory and for their assistance in so many ways throughout the progress of this study.

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5. The risk of ventral hernia and postoperative adhesions is eliminated.
6. Adequate drainage more easily secured.
7. Less risk of injury to bladder and ureters, providing the bladder is properly freed and elevated at the beginning of the operation.

W. Wayne Babcock⁴ reported 300 vaginal hysterectomies without a death. N. Sproat Heaney⁵ reported a series of 627 vaginal hysterectomies with a mortality of 0.47 per cent. Kennedy reports a mortality of one-fifth of 1 per cent in several thousand cases.

Our own series consists of 348 cases without a death.

TABLE I. AGE INCIDENCE

9 between ages of	20 to 29
84 between ages of	30 to 39
174 between ages of	40 to 49
60 between ages of	50 to 59
18 between ages of	60 to 69
2 between ages of	70 to 79
1 between ages of	80 to 84

The two oldest patients in this series deserve special mention.

One patient seventy-eight years of age was admitted, suffering from profuse uterine hemorrhage and intermittent uterine contractions. Upon vaginal examination, the vagina was found to be filled with clots, the cervical canal was patulous, the uterine cavity measured 12 cm., and a submucous fibroid, the size of a hen's egg, was attached to the fundus.

Another patient eighty-four years of age was admitted with a complete procidentia and hemorrhage from an ulcerated cervix requiring packing to control the bleeding.

TABLE II. INDICATIONS

Fibromyoma of the uterus	193
Fibromyoma of the uterus fixed to anterior abdominal wall by previous operation	5
Fibromyoma of the uterus and bilateral chocolate cysts of ovaries	2
Fibromyoma of the uterus and ovarian tumors	8
Fibromyoma of the uterus and chronic bilateral tuboovarian disease	12
Hyperplastic or fibrotic uteri with excessive bleeding about the menopause	68
Prolapsus of uterus	51
Prolapsus of uterus with advanced carcinoma of cervix	1
Prolapsus of uterus after an interposition operation	1
Badly lacerated, diseased cervix	6
Adenomyoma of the uterus	1

Vaginal hysterectomy was performed sixty-eight times, in our series, for functional uterine bleeding in middle-aged women.

G. I. Strachan⁶ reports two cases of functional uterine bleeding, proved to be benign by curettage, and the patients later developed cancer of the body of the uterus, seven years and two years, respectively, after the use of radium.

cystitis. He attributes these to mucosal disease of the cervix. The organism in the cervical mucosa while ordinarily attenuated may become activated and markedly pathogenic. This is further proved by the frequent incidence of secondary septic hemorrhage following trachelorrhaphy or trachelectomy which generally occurs on the eighth or twelfth day, the hemorrhage at times being severe enough to require transfusion.

The advocates of the subtotal or supravaginal hysterectomy claim a smaller mortality and a lesser morbidity as compared with the total or panhysterectomy. The advocates of the total hysterectomy claim that, in the first place, in expert hands the mortality and morbidity are not any greater, and second, the elimination of the possibility of cervical stump cancer and focal infection make this a more advantageous operation. Their claim is supported by statistics such as those of Fullerton and Faulkner,³ who reported 1,851 abdominal hysterectomies, subtotal as well as total, with a mortality rate of 4.5 per cent. Sixty-three per cent of the 1,078 total hysterectomies were performed by five members of their visiting staff and the mortality was 3.5 per cent, while in 37 per cent performed by two members of the resident staff, the mortality was 5.2 per cent.

At a recent meeting of the Southern Medical Association in Baltimore, Q. V. Newell read a paper in which he summarized the mortalities in his cases.*

	MORTALITY
Supravaginal hysterectomy in cases complicated by pelvic infection	4.2%
Total hysterectomy in cases complicated by pelvic infection	3.2%
Supravaginal hysterectomy in cases not complicated by infection	3.5%
Total hysterectomy in cases not complicated by infection	1.3%

He reviewed the literature for a five-year period and compiled a total of 14,280 supravaginal hysterectomies with a minimum mortality of 1.2 per cent and a maximum one of 4.7 per cent. A similar summary of 5,223 total hysterectomies showed a minimum mortality of 1.0 per cent, and a maximum of 7.9 per cent.

Vaginal hysterectomy accomplishes everything claimed for the total abdominal hysterectomy, and has the following advantages over the abdominal hysterectomy:

1. Lower operative mortality and morbidity.
2. Less tendency to peritoneal infection or shock and is therefore suitable in cases that are bad operative risks and in no way a disadvantage to the robust patient.
3. In the treatment of hemorrhagic conditions of the uterus in middle-aged women, the mortality rate in vaginal hysterectomy is as low as that of radium, without the sequelae and relapses; furthermore, possible malignant conditions are, in the former procedure, readily disclosed and eliminated.
4. Convalescence is rapid, the patient is able to eat breakfast and read the daily paper the morning after operation. When hysterectomy alone is done without extensive plastic work the patient is practically devoid of complaint.

*Personal communication.

The indications for vaginal hysterectomy increase and the contra-indications diminish with the increased skill and experience of the operator. Thus far we have not had to abandon the vaginal route and complete the operation abdominally. In difficult cases, the abdomen is prepared for just such an emergency. Following Dr. Babcock's description on morcellation of large fibroids, we were able to remove fibroids reaching above the umbilicus through the vaginal route.

A skillfully executed vaginal hysterectomy is a decidedly less formidable procedure as determined by its demonstrable effects upon the patient than is the same operation performed with equal skill by the abdominal route.

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2106 SPRUCE STREET

DISCUSSION

DR. W. WAYNE BABCOCK.—By using clamps one may remove the uterus in the quickest time and in the simplest manner. Clamps, however, limit the field of vaginal hysterectomy. When they are used it is difficult to take out a large uterus or a complicating ovarian tumor, and they interfere with an associated vaginoplastic operation. If a clamp rests against the soft tissues during the conventional forty-eight hours that it should be left on, it will cause a slough. Therefore, one should always carefully protect the vaginal wall by gauze packing. Occasionally a secondary hemorrhage follows the removal of the clamps.

After several alarming hemorrhages I turned from clamps to mass ligatures on the broad ligaments. Experience proved these to be insecure, a uterine artery or other vessel occasionally escaping from constriction during the extrication of the uterus. An associated closure of the vaginal vault also proved to be unwise probably because the pedicles were not anchored extraperitoneally, and not infrequently led to a pelvic abscess about the time the patient should have been ready to leave the hospital.

I therefore found it wise to expose and ligate the uterine and ovarian vessels individually on the sides of the uterus. This enabled me to open the anterior and posterior culdesac without any special effort, for the peritoneum is incidentally penetrated at the side of the uterus while exposing, ligating, and dividing the vessels. Thus there was little danger of injuring the bladder or rectum, and by proper retraction with a small trowel, the ureters are not endangered. The vaginal vault was also left open and a Mikulicz drain carried into the pelvis. This did away with the secondary pelvic abscesses, but in three instances, intestinal adhesions to the gauze or some adjacent part led to an obstruction requiring secondary operation. We, therefore, then brought the pedicles through the peritoneum to the vaginal wall where they were anchored, the peritoneum being closed, and the vaginal margins lightly approximated over the pedicles. Thus far this method has worked well.

With large fibroid tumors, for we remove fibroid uteri up to the size of a seven months' gestation, much of the blood supply is controlled before the morcellation is started and therefore there is less loss of blood. With the abdominal walls relaxed and the patient in a high Trendelenburg position, the interior of the pelvis and

Vaginal hysterectomy was performed in five cases of fibromyoma where the uterus was fixed to the anterior abdominal wall by previous operation.

TABLE III. ADDITIONAL OPERATIVE PROCEDURES

Removal of one or both tubes	62
Removal of one or both ovaries	42
Plastic on urethra for incontinence	23
Posterior colpoperineorrhaphy	296
Repair of complete perineal tear	1
Preliminary episiotomy	26
Removal of Bartholin cyst	2
Repair of inguinal hernia	3
Repair of umbilical hernia	3
Appendectomy	2

With a virginal, nulliparous or atrophic vagina, a simple median episiotomy was performed. We have found no necessity for the extensive lateral incision of Schuchardt.

TABLE IV. PREOPERATIVE COMPLICATIONS

Secondary anemia, hemoglobin below 60%	42
16 required transfusion	
Hypertension (systolic pressure above 150)	61
Chronic nephritis	18
Pulmonary tuberculosis (arrested)	3
Diabetes	5
Valvular heart disease	4
Chronic myocarditis	16

Among the sixteen patients requiring preoperative transfusions, one had a hemoglobin of 27 per cent with 1,218,000 red blood cells per cubic centimeter. This patient and three others required three transfusions each. Five patients required two transfusions each.

The metabolist was called in to treat the diabetic patients.

TABLE V. POSTOPERATIVE COMPLICATIONS

<i>Temperature over 100.6° for one or more days due to:</i>	
Femoral thrombophlebitis	8
Cystitis	19
Probably due to wound infection, low grade	32
Tonsillitis	2
Bronchitis	3
Deaths	0

TABLE VI. OPERATION

Type:		
Ligature		172
Clamp and ligature		62
Mayo modification		76
Kennedy clamp method		38
Anesthesia		HOSPITAL DAYS
Spinal	312	14.6
Gas and ether	36	

ON THE ORIGIN OF THE SUBSTANCE IN URINE WHICH PRODUCES ELONGATION OF THE BITTERLING OVIPOSITOR

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IT IS generally agreed that the ovipositor of the bitterling will elongate if a small quantity of urine from normal men, pregnant women, and many nonpregnant women, is added to the water in the aquarium. Three theories have been advanced to explain the occurrence of this active substance which, for brevity, will be designated ovipositor lengthening substance in this report. The ovaries, the testes, and the adrenals have been suggested as possible sites of production of the compound (or compounds) responsible for the reaction. In the present report a brief discussion of the evidence for each theory is presented and experimental observations on the subject are recorded.

The ovarian theory (Fleischmann and Kann¹) was based upon the observation that injection of commercial estrogenic preparations into the bitterlings caused the ovipositor to lengthen. Many investigators have made similar observations upon adding estrogenic preparations to the aquarium.

It seems unnecessary to review the extensive literature which followed and only a few papers will be cited which, in our opinion, make it improbable that the activity of the urine is due to estrogenic substances.

Ehrhardt and Kuhn² found no correlation between the ovipositor lengthening substance and the estrogenic activity in human blood, human urine, and pregnant mares' urine. They further observed that the more refined estrogenic preparations were less effective on the bitterlings. This observation was confirmed by Kanter, Bauer, and Klawans.³ We realize that samples of urine which give a positive effect could not contain the quantity of crystalline theelin necessary to cause a similar reaction in the fish. Kleiner, Weisman, and Mishkind⁴ made the further observation that by fractionation the estrogenic activity in urine could be separated from the ovipositor lengthening substance. Kanter, Klawans, and Barnes⁵ obtained negative results with ether extracts of fresh ovaries. In view of the evidence at the present time, it seems improbable that the ovipositor lengthening substance originates in the ovaries.

Glaser and Haempel⁶ observed that preparations of male hormone would also cause the bitterling ovipositor to lengthen and pointed out that the reaction was nonspecific. These observations have been confirmed recently by Kleiner, Weisman, and Mishkind⁴ who believe that the bitterling reaction can be used as a method of assay for male hormone. Their evidence for the testicular origin of the ovipositor

lower abdomen may be inspected after the uterus has been removed. While as yet we have not been able to see the gallbladder, we have removed the appendix through the vagina, in about eighty such cases. Without clamps one or both ovaries may be resected or removed, and an anterior colporrhaphy and perineorrhaphy conveniently done after removal of the uterus.

To one experienced vaginal hysterectomy is the safest method of complete removal of the uterus, although not always the easiest for the operator. How else can one maintain a mortality under 0.5 of 1 per cent? It also has the lowest morbidity. If no vaginal plastic is done, the patient may be out of bed on the sixth day, and leave the hospital, without the cares of complications of an abdominal incision, on the eighth or tenth day. In the vaginal repair, we have found buried fine rustless steel wire of advantage. It is tieable, much stronger than silver wire, and need not be removed.

DR. HILLEL (Docent of the Mackenrodt Clinic, Berlin).—The first vaginal operations I saw were performed by Mackenrodt and Dührssen. If they could see the field which vaginal operations have attained in America, they would be astonished. In former times America could learn from Europe, but the surgery I have seen here in the United States has reached such a high standard that I believe Europe has nothing to offer any more.

DR. J. W. KENNEDY.—Thirty-odd years ago in the Joseph Price Hospital 50 per cent of the hysterectomies performed were done by the abdominal route. Today 5 per cent are performed through the abdomen against 95 by vaginal hysterectomy.

The indications for the operation are: All fibroid tumors that can be removed by the vaginal route and, if morcellation is resorted to, large growths may be removed through the vagina; all dysfunctions of the uterus in the suspicious and sterile uterus; all degrees of prolapse of the uterus in the sterile organ; all conditions of the abused cervix in patients over forty-five; in all patients where malignancy comes within the first and second groups; in all polypoid growths of the cervix in patients over forty-five, as over sixty per cent of these patients will show similar growths of the fundus, and in practically all patients with excessive weight with cardiorenal symptoms.

We feel that the slough incident to the clamps is a very important factor in the recommendation of the procedure in malignancy of the uterus.

The clamp method in removing the uterus is most important in any degree of prolapse of the organ, for after the clamps are removed the broad ligaments contract and pull the vaginal fornix high up and thus relieve the prolapse which takes care of the cystocele in most conditions. In the extensive prolapsed conditions, such as complete procidentia, we immediately do a repair of the cystocele by the use of silkworm-gut sutures.

The slough incident to the clamp method of removing the uterus causes an infectious discharge and buried absorbable sutures must not be used.

The mortality of vaginal hysterectomy is the lowest of any major operation of which I have knowledge. I have never seen a death from operative infection, operative or postoperative hemorrhage, nor from an embolus or postoperative pneumonia.

The clamp method of removing the uterus lengthens the vagina, the ligature method shortens it. The use of the clamps gives a large percentage of operability. The operative time is the shortest of any major operation of which I have knowledge. Very often the anesthesia may be stopped when the operator begins the procedure. There is little shock in vaginal hysterectomy.

known to give a positive reaction, and in no case were the fish found to be refractory to active material (adrenal extracts).

The first fresh tissue extracts were carried out on an immature female dog. The animal was killed with chloroform and the tissues quickly removed and extracted according to the above procedure. The following tissues gave negative results with the quantities employed: brain 20 gm., muscle 20 gm., kidney 20 gm., heart 20 gm., liver 20 gm., stomach 20 gm., lung 20 gm., pancreas 13.4 gm., spleen 9.2 gm., thyroid 1.4 gm., thymus whole gland, and pituitary whole gland. The adrenal from the same animal was positive using 0.7 gm. The endocrine organs from a large male dog gave similar results; the testes weighing 22 gm. were negative and the adrenals weighing 1.3 gm. were positive. Since the adrenal extracts were strongly positive, similar preparations were made from various species. Table I illustrates the results.

TABLE I. SHOWING THE REACTION OF THE JAPANESE BITTERLING TO EXTRACTS OF THE ADRENAL GLANDS FROM VARIOUS SPECIES

SPECIES	ADRENAL WEIGHT	REACTION
Dog	0.7 gm.	+
Dog	1.3 gm.	+
Cat	0.75 gm.	+
Rat (63 animals)		+
Guinea pig	1.0 gm.	+
Beef*	0.5 gm.	-
Beef	1.0 gm.	+
Human being	About 1.0 gm.	+

*We are indebted to Dr. Fenger of Armour and Co. for a generous supply of fresh beef adrenals.

In all the species investigated thus far the adrenals have yielded positive results when approximately 1 gm. of adrenal was employed. In over 30 human cases coming to postmortem,* the adrenals have been positive, with two exceptions, when 1 to 2 gm. of adrenal were employed. Both of these patients died from lobar pneumonia and the adrenal extracts were negative when 5 and 6 gm., respectively, were tested. The age of these human cases varied from stillbirth to sixty-nine years. Quantitative variations with age and disease are now being investigated.

At the present time it is impossible to say whether the ovipositor lengthening substance is present in the cortex, in the medulla, or both. One adrenal at autopsy presented a cortical adenoma, weighing 2 gm. It was carefully shelled out from the gland and extracted with ether. Positive results were obtained with the equivalent of 0.5 gm. of fresh tumor. This is slightly more potent than whole glands but more careful quantitative estimations are necessary before any conclusions can be drawn.

After a high content of ovipositor lengthening substance in the adrenals was found, attention was directed to the excretion of the compound in cases with adrenal pathology. The urine from five cases of Addison's

*The cooperation of Dr. R. L. Jaffe and his assistants at the Cook County Morgue is greatly appreciated for the autopsy material.

lengthening substance is: (1) Crude fractions of urine containing (among other substances) androgenic activity are highly potent on the fish.

(2) Crystalline androsterone in doses of 0.8 to 1.2 mg. causes a delayed reaction on the fish.⁷

Crude extracts can do little more than confuse the investigator; hence the first evidence is not convincing. Regarding the second observation, there seems to be the same quantitative discrepancy between the ovipositor lengthening substance in the urine and the androgenic activity as there was between the ovipositor lengthening substance and the estrogenic content. In a later paper Kleiner, Weisman, and Mishkind⁸ report the daily excretion of 35 to 40 bitterling units in the urine of normal men. If this activity were due to androgenic activity and 1 mg. (0.8 to 1.2 mg.) of androsterone were necessary for the bitterling reaction, it would necessitate the daily excretion of 35 to 40 mg. of androsterone or its equivalent. This is several times the daily excretion found by Gallagher, Peterson, and Koch.⁹ Hence, until this quantitative discrepancy can be explained, we must discount the evidence in favor of the testicular origin of the ovipositor lengthening substance in urine. Evidence against the theory will be presented in this report.

The third theory (adrenal) was suggested by the observation of Barnes, Kanter and Klawans¹⁰ using ether extracts of fresh tissues. The adrenals contain large quantities of a substance causing elongation of the bitterling ovipositor while other tissues, including the gonads, are relatively inert. The details of these experiments and further evidence in favor of the adrenal origin are presented below. It is fully realized that the evidence for the identity of ovipositor lengthening substance in the urine and in the tissues is purely circumstantial. It is well known that both the male hormone and female hormone occurring in the urine are different compounds from those occurring in the respective gonads. The same may prove true of the ovipositor lengthening substance.

EXPERIMENTAL

The search for the source of ovipositor lengthening substance began with the extraction of fresh tissue with ether. The procedure followed in these experiments was to mince fresh tissues and extract with about five volumes of ether for twenty-four hours or longer. The ether or a portion of it was decanted into a dry fish bowel and allowed to evaporate. A liter of water was added and usually two bitterlings. The ovipositor was observed at twenty-four, forty-eight, and seventy-two hours, and only those recorded as positive which had elongated beyond the end of the ventral fin. In most cases this represented an increase of 100 per cent or more in the length of the ovipositor. This avoids any possibility of confusing slight spontaneous changes with positive results. Whenever negative results were obtained, the fish were then tested with material

Table II illustrates a series of cases in which the adrenal and the gonad were extracted in the same case.

TABLE II. SHOWING THE REACTION OF THE JAPANESE BITTERLING TO EXTRACTS OF THE ADRENALS AND GONADS

CASE	SEX	AGE	GONAD		ADRENAL	
			GM.	RESULT	GM.	RESULT
425	F	26	6	-	4.0	+
469	F	23	12	-	2.5	+
509	F	-	8	-	2.0	+
545	F	29	18	-	2.0	+
423	M	60	28	-	10.0	+
468	M	65	19	+	1.5	+
471	M	33	12	+	2.0	+
472	M	69	33	-	1.0	+
488	M	47	17	-	2.0	+
502	M	52	15	-	1.0	+
504	M	27	8	+	1.0	+
			6	-		
532	M	61	8	-	6.0	-
537	M	58	17	+	1.0	+
			8	-		
546	M	36	32	-	2.0	+
548	M	50	15	-	2.0	+
553	M	49	25	+	2.0	+

The results on the ovaries were consistently negative even though as much as 18 gm. of tissue were employed. The results using the testes were quite variable being negative in 7 and positive in 5 cases. However, in 2 cases giving positive results with 8 and 17 gm., respectively, the same extracts were negative when 6 and 8 gm. of testes were used. Thus, it appears that although some cases of human testes contain a substance which causes the bitterling ovipositor to lengthen, the concentration is much less than in the adrenal of the same individual.

We have no evidence as yet for or against the identity of the active material from the testes and from the adrenals. We were interested, however, to see if the active fraction from the adrenal could be attributed to androgenic substances. Two preparations known to be highly active on the fish were tested on capons. A sample of "adrenal cortex extract" supplied through the generosity of Dr. Kline of Wilson Laboratories, Chicago, was found to give a positive response in the fish when 0.25 c.c. was added to the aquarium water. The same specimen had no influence on the capon comb when 40 times this quantity was injected over a period of five days. Similar results were obtained with the beef adrenal extract referred to in Table I. The ether extract was concentrated, olive oil was added and the remaining ether driven off with heat. Injection of 200 times the fish dose gave no effect on the capon comb. It would appear that the activity of the adrenal extracts is not due to androgenic activity. Since preparations from several different sources cause the bitterling ovipositor to lengthen, this reaction seems unreliable as a test for specific hormones at the present time.

disease was tested on the fish and found to contain less than one-half the normal quantity of ovipositor lengthening substance. During a reexamination, one of these patients was receiving 10 c.c. daily of commercial adrenal cortical extract at which time a normal excretion of ovipositor lengthening substance was observed. We have not been fortunate enough to encounter a case of adrenal tumor before autopsy, but in view of the result on the extract of the cortical adenoma, an increased excretion is anticipated. The excretion of ovipositor lengthening substance in health and disease is being investigated.

The recent isolation of crystalline compounds from the adrenal made it possible to test their activity without danger of contaminating impurities. Dr. E. C. Kendall kindly sent us samples of his compounds A, B, and E.¹¹ Small quantities of each were weighed out on an analytical balance, transferred to a fish bowl, and a liter of water plus two fish added. Positive results were obtained with 0.18 mg. of A, 0.27 mg. of B, and negative results with 1.2 mg. of E. The question of insolubility of compound E must be ruled out when more of it is available. The quantity of A and B necessary for a fish reaction is far less than any compound tested thus far. It seems better to record the observations at this time and wait for explanations until other compounds from the adrenal and from urine have been tested.

The above experiments are the basis for our theory that the ovipositor lengthening substance in urine originates in the adrenal. Although the positive effects of extracts from fresh adrenals, the decreased excretion in Addison's disease, and the high potency of crystalline compounds from the adrenal are all indirect evidence, it seems more logical than the evidence for either the ovarian or the testicular theory. A few observations have been made which indicate that the bitterling reaction would be wholly unreliable as a test for male hormone. The quantitative discrepancy between the androgenic activity and the bitterling activity of urine has already been discussed. In our own experiments we usually obtain a positive fish test when 4 c.c. of normal male urine are added to one liter of water. Our negative result¹⁰ using androsterone* was probably due to an inadequate dosage. Although we used a quantity far in excess of that contained in 4 c.c. of male urine, it was less than 0.8 mg. which was the minimum in the experiments of Kleiner and others.⁷

If the bitterling activity in urine were due to androgenic substances alone, a decreased excretion should be expected in the castrate male. We have examined only one case, a vigorous young male castrated over three years previously. (This specimen was obtained through the courtesy of Dr. C. F. Read of Elgin, Illinois.) The excretion of ovipositor lengthening substance in this case was normal. Similar cases are being sought. The extractions of fresh human testes have yielded inconsistent results.

*We are indebted to Dr. T. F. Gallagher for the crystalline androsterone.

AN EVALUATION OF COMMON CERVICAL LESIONS

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EVER since Thomas Addis Emmet, more than sixty years ago, called attention to cervical lacerations as a cause of uterine disease, there has developed a growing and widespread interest in the uterine cervix and its disorders. Many conditions have been recognized and described. The basis for establishing their pathologic nature and disease producing propensities was the limited knowledge available at the time. Now, in the light of newer discoveries, it appears that certain deductions of our predecessors, generally accepted today, may be in need of revision.

Included under the term common cervical lesions are: Cervicitis, erosion, cystic changes, polyps, leucoplakia, lacerations, and eversions.

The clinical picture and histologic changes characterizing these abnormalities have been reported voluminously in the literature and are probably well known to most practitioners. Indeed, it is the unusual physician's office that cannot boast of at least one pet therapeutic measure or mechanical apparatus for their control and cure. To be properly evaluated these common lesions should be seen in the light of their immediate danger as well as from the standpoint of their remote disease producing possibilities. Thus, each lesion may wisely be considered from the standpoint of its ability to: (1) Cause or predispose to cancer; (2) act as a focus for infection; (3) produce local symptomatology; (4) prevent conception, i.e., be a factor in sterility; and (5) cause cervical dystocia.

More and more, physicians have come to see in these common disorders the foreshadowing of serious disease later in life. This attitude and the associated universal tendency to treat such disorders has undoubtedly resulted in benefit to womankind and today, would seem to present an ideal situation. Such growing concern, however, has not been entirely an unmixed blessing. The ease with which the cancer conscious woman falls prey to the implication of future malignancy is becoming more and more a convenient wedge for radical therapy. Too often concern for the patient's future is but a handy motive for major pelvic surgery. No one can deny that removal of the cervix will prevent future disease of that organ but in many instances we may seriously question the need for and wisdom of so doing. Cervical prophylaxis like a therapeutic dose of strychnine is often desirable, but overtreatment of the cervix, like an overdose of strychnine, is likely to be harmful. This growing tendency to radical therapy of the cervix is only one reason why a re-evaluation of the common cervical dis-

SUMMARY

The following experimental observations are reported:

1. When various fresh tissues were extracted with ether, only the adrenal extracts consistently caused the bitterling ovipositor to lengthen. Several species were investigated and the adrenals were positive in each instance.

2. The only other tissue which caused a positive reaction was the testis, positive in 5 of 12 cases. However, the quantity of fresh tissue necessary was several times greater than with the adrenals from the same case.

3. Crystalline compounds isolated from the adrenal were comparatively more effective than androsterone.

4. In 5 cases of Addison's disease a decrease was observed in the excretion of the ovipositor lengthening substance.

5. No decrease was observed in the urine of a castrated male.

6. Extracts from the adrenal causing the fish reaction had no influence on the capon comb in doses 40 to 200 times greater.

The evidence indicates that the adrenal must be considered as one possible source of the factor in urine which causes the bitterling ovipositor to lengthen.

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The author following the work of Ascoli and Vercesi and the experimental work of Ducceschi undertook the transfusion of placental blood. The blood is collected from the cord immediately upon the birth of the child, is mixed with an equal part of Ringer's solution, to which is added 1.5 per cent of pure formalin for preservation. After using this solution for transfusion in rabbits and obtaining satisfactory results the author then used it for transfusion in a very ill patient who had advanced carcinomatosis.

After the first transfusion of 100 c.c. in the above mentioned case the patient, who had no reaction from the procedure, had a very much improved appearance and a marked feeling of well being. The author on this clinical evidence then attempted a second transfusion; after injecting 30 c.c. of the fluid the patient reacted badly and the transfusion was stopped. The procedure was not repeated.

The author concludes that more work should be done along this line to the end that it may be of clinical value.

MARIO A. CASTALLO.

during the gravid and puerperal states are reasonably well known. The periodic response of the endometrium to hormonal stimulation is no longer a controversial matter. That the squamous epithelium of the vagina is also subject to this hormonal influence is a more recent observation. As part of the uterus and of similar embryologic origin it would not be unreasonable to expect some such functional activity in the epithelium lining the cervical canal.

The recent work of Wollner¹⁶ seems to leave little doubt regarding such periodic activity. According to Wollner's observations the columnar epithelium of the cervical canal undergoes cyclic changes which are very similar to those seen in the endometrium each month. There is hypertrophy, hyperplasia, desquamation, and associated secretory activity of the cervical glands. This physiologic activity of the columnar and glandular epithelium plus certain clinical evidence suggests a new etiology and interpretation for cervical erosions. Few older gynecologists have forgotten the pathologic interpretation once given the normal secretory phase of the endometrium. That which we recognize today as merely a phase in the normal physiology of the endometrium was considered a pathologic entity but a few decades ago. The importance of knowing the physiology of an organ before describing its pathology needs no comment. We believe it is not unreasonable to assume that a *cervical erosion represents an enthusiastic response of the endocervium to hormonal stimulation*. We doubt its explanation on the basis of cervicitis, although it may be associated with infection. This origin is suggested by newer knowledge regarding cervical physiology and also by certain clinical observations. For example, cervical erosion is uncommon after the menopause and its associated hormonal decline. Erosions are frequently seen in young women. The so-called congenital or pseudo-erosions are common examples. Furthermore, many patients with cervicitis show no evidence of erosion and the reverse is also true. Certainly there appears to be no consistent etiologic relationship between cervical infection and erosion. While convincing proof is necessary we believe this common disorder likely to be in the nature of an over-responsive physiologic manifestation calling for new clinical interpretation. Roblee²³ recently suggested that erosions occur as a result of increased alkalinity due to greater cervical secretion. While this may be an important factor in causing an environment favorable to the spread of columnar epithelium it would seem that hyperplasia of the endocervium, probably due to hormonal stimulation, is more likely to be the basic cause.

For many years we have accepted without question a definite cause and effect relationship between the cervical disorders and cancer. So strong is the feeling regarding this relationship and so extensive the compiled indirect evidence that, to think otherwise, is likely to be considered rank heresy. Yet when viewed in the light of present-day knowledge there is reason for doubting the amplitude of this relationship. It is not our intention to minimize the wisdom of reasonable cervical prophylaxis. We believe in it. Yet, if we are to arrive at a true understanding of cervical pathology in relation to cancer it is necessary that we weigh

orders appears necessary. Other significant reasons are the newer knowledge regarding physiology of the cervix, its apparent response to hormonal stimulation and the increasing clinical evidence contradicting a cause and effect relationship between most common cervical disorders and cancer. For these reasons we believe a re-evaluation of the common cervical disorders is needed. It is time we placed our ideas regarding them back into the melting pot, there to be freely mixed with newer knowledge. By so doing we may hope for either verification of existing concepts or new interpretations based on all available evidence, both old and new.

While complete re-evaluation appears desirable we shall limit this paper to an explanation for cervical erosions and a consideration of the cause and effect relationship between cervical disorders and cancer.

Since cervical epithelium plays such an important part in cervical morbidity we may well begin by looking into their origin or embryology.

ORIGIN OF CERVICAL EPITHELIUMS

There are two current theories pertaining to the origin of the upper portion of the vagina and its epithelium which in the adult is identical with that covering the vaginal face of the cervix. Briefly, these theories are (1) Müllerian duct origin (mesoderm) and (2) from the outside by a proliferation from the urogenital sinus.

In support of the former theory the work of Hunter² and Koff³ as the most recent investigators, is outstanding. Briefly, they maintain that the Müllerian ducts, which originate in the body (celomic) cavity on either side just lateral to the primitive kidney (mesonephros or Wolffian body) burrow their way posteriorly. Finally they reach the surface (urogenital sinus) and fuse. This fusion continues upward to a point which represents the future fundus of the uterus, the remaining portions become the Fallopian tubes.

The cervix is eventually formed from a portion of the fused tubes while the upper vagina arises from a small nest of cells just distal to the cervix.

Koff and Hunter agree on the formation of the upper vagina but disagree on the lower portion. The former believes that the lower one-third develops from the outside, while the latter claims the entire vagina is Müllerian in origin.

The theory that the cervical epithelium arises from the outside, is largely supported by Meyer⁴ and Schubert.⁵ Their work is based on extensive study of malformations of the generative tract in the fetus and adult.*

All agree on the subsequent course of development characterized by a rapid proliferation of the cells described as the primordia of the vagina. These form a solid cord, the central cells of which slough, forming a tube lined by squamous epithelium. This epithelium extends up to the external os where there occurs an abrupt change to the secretory columnar epithelium of the endocervix. Fundamentally it appears that all cervical tissues are of mesodermal origin. This common source of the generative tract epithelia may help explain certain changes which we now view with concern.

PHYSIOLOGY OF THE CERVIX

Our knowledge of cervical physiology has been limited to its connection with childbearing. Its gross changes and functional activity

*The reader interested in embryology of the female generative organs is referred to the monographs on the subject by these men.

are on the decline, as the cancer incidence rises. The significance of metaplasia in the cervix has not been definitely determined but its serious import appears unlikely.

Overholtser and Allen,¹⁹ Engle and Smith,²⁰ Hisaw and Lendrum²¹ have caused benign metaplastic development of squamous epithelium in the cervical glands of monkeys by the administration of estrin. Fluhmann¹⁴ has found similar changes in the epidermidalization of the human cervix but believes the majority of these changes to be harmless.

Hinselmann¹³ is probably responsible for much of the present interest in cervical leucoplakia. Doubtless most gynecologists have toyed with the thought of adopting his colposcopic methods as part of their routine. Our own experience with the colposcope has proved an intriguing, time-consuming, and not too illuminating procedure, but it has led to greater interest in cervical morbidity. The term leucoplakia is generally applied to any thickened, whitish hyperkerototic area on the cervix. Novak¹⁷ explains the simpler grades on the basis of differentiation anomalies and is not greatly disturbed over their presence. He is, however, concerned with the forms (Hinselmann rubric III) showing cell anaplasia and sometimes called intraepithelial carcinomas. Such finely drawn differentiation based on microscopic study is not very helpful to us as practitioners, and it would seem that if certain forms of cervical leucoplakia are dangerous from the standpoint of cancer development, then closer scrutiny and more attention should be paid to all cervical leucoplakias. By analogy, one may reason that, if leucoplakia elsewhere on the body is known to predispose to malignancy, then why not leucoplakia of the cervix also? Certainly we view with suspicion leucoplakic lesions of the mouth or vulva, why should we not look with apprehension on similar conditions of the cervix?

With the increasing importance attached to cervical prophylaxis as a means of cancer prevention, it is imperative that we try to determine more accurately which lesions are harmless and which are to be subjected to radical therapy. Obviously every woman past thirty years of age cannot and should not be subjected to cervical amputation. The continued high incidence of cervical cancer in spite of widespread prophylaxis in thousands upon thousands of patients now extending over several decades would seem to indicate that we may be attaching too much significance to these easily recognized conditions and neglecting others.

Finally, we cannot overlook the fact that Jewish women seldom develop cervical carcinoma. Yet, they are by no means immune to the common cervical disorders under consideration. While this must be looked upon as a racial difference in disease incidence, it also emphasizes the fact that a positive cause and effect relationship between the commonly recognized cervical disorders and cancer is by no means proved.

SUMMARY

While there are no conclusions to be drawn from this discussion, certain points may be restated thus:

1. There is need for re-evaluation of the common cervical disorders.

all the evidence. No need to detail the many arguments favoring such cause and effect relationship. These have been abundantly recorded and are well known. Arguments against such relationship are neither numerous nor yet convincing but are becoming increasingly so. While cervical erosions are today considered particularly offensive in this respect, not one of the common conditions mentioned has escaped implication.

For years cervical cancer and childbirth trauma have commonly been mentioned in the same breath. The existence of a close relationship between tears and cervical cancer has become a foregone conclusion. *Yet, it is remarkable that in a study of many hundreds of cervical cancers we should rarely find the carcinoma developing at the site of the old tear.* Indeed we have come to view the average old cervical tear as no more significant than any other ordinary scar elsewhere in the body.

Natale¹⁸ in a study of 879 cervical carcinomas occurring in Milan found that 15 per cent or, excluding the unmarried, 11.84 per cent were in nulliparas. This would agree with the existing concept that about 90 per cent of cervical cancers occur in parous women. But, this is only part of the story, for Natale also found that only 11.8 per cent of the married women in Milan over forty years of age were nulliparas. If further study corroborates Natale's findings, the significance of child-bearing as predisposing to cervical cancer will be dealt a severe blow. Suggestive in this connection, particularly in the light of Natale's report, is the fact that for the year 1931, 12 per cent of the deaths from cancer of the uterus (cervix and corpus) in the United States registration area were in single women. For the same year 17 per cent of the deaths from this source in the State of Michigan were among single women. Unfortunately, we are unable to ascertain the number of nulliparas over forty years of age in these areas for the year mentioned.

The important relationship between chronic irritation and cancer is a proved fact, but whether the irritation associated with common cervical lesions is of the proper type is another matter. In this connection cervicitis has been considered particularly significant and well it may, for it is an important and very common disorder. Yet, speaking generally, inflammatory irritation in other parts of the human body reveals no unusual cancer producing propensities. The chronically infected sinus, appendix or Fallopian tube, seldom undergoes neoplastic change in spite of prolonged irritation of inflammatory character. The kinship between cervical carcinoma and cervicitis through the medium of an erosion has been particularly emphasized. As previously stated we doubt the generally accepted inflammatory origin of cervical erosions. Furthermore, the monographs presented in proof of an erosion to cancer relationship are far from convincing. It is perhaps not so difficult to understand why 90 per cent of cervical cancers are of the squamous and not columnar cell variety, but it is difficult to reconcile the fact that cancer is seldom seen to develop in an erosion. Furthermore, erosions

isolated from the vagina of infected puerperal cases, yet few workers have reported the incidence of this organism in the vagina in healthy pregnant women. Many claim that the Welch bacillus is rarely, if ever, found in the genital tract without gross infection. Lindenthal, in 1897, reported the presence of gas bacilli in two out of six puerperal patients, none of whom gave clinical evidence of infection with the gas bacillus. Later, Schottmüller stated that occasionally the organism could be found in the vagina of normal healthy women. Reporting anaerobic vaginal cultures from a large series of prenatal patients, Falls showed an incidence of *B. welchii* in 6.25 per cent of the cases.

From these early reports it can be concluded that the presence of *Cl. welchii* in the genital tract does not necessarily signify infection.

It is possible that the Welch bacillus in symbiosis with another organism may favor the growth and increase the virulence of either invader. The gas bacillus may be considered a saprophyte, gaining pathogenicity only when growing in the presence of devitalized tissue. Such conditions are frequently presented in the genital tract by prolonged labors and difficult deliveries. Obviously such factors as the resistance of the patient and the virulence of the organism play an important rôle. The bacterial flora of the vagina during pregnancy does not differ greatly from that of the normal vagina; certainly new species are not usually added in the pregnant state. The presence of any potentially virulent organism such as the Welch bacillus in the genital tract of a pregnant woman indicates an increased possibility that that woman may develop puerperal sepsis.

As far as true gas bacillus infections in pregnancy are concerned, Welch was again the first to classify the types of infection caused by this organism. Pathogenically the *Bacillus aerogenes capsulatus* may give rise to: (a) emphysema of the dead fetus, (b) puerperal endometritis, (c) physometra, (d) emphysema of the uterine wall, and (e) gas bacillus sepsis. The dramatic clinical picture of fever, toxemia, cyanosis, jaundice and prostration, culminating in the rapid exodus of the patient is explained by the exotoxins produced by these bacteria. These toxins manifest themselves as myotoxins and hemotoxins. It is the opinion of Wrigley that gas bacillus uterine infections are more common in septic abortions than in full-term deliveries. At term, the death of the fetus some time before delivery, plus damaged maternal tissues, and introduced infection, are the prerequisites for a true *Cl. welchii* infection. He also states that the gas bacillus is not found in the vagina or cervix of normal cases, nor in these sites in labor, nor in the normal lochia. Wrigley does maintain, however, that anaerobic cultures are not used often enough. In 69 cases of abnormal pregnancy, labor, and puerperium, he was able to find Welch bacilli in the lochia of 13 patients. The above statements lead to the conclusion that infected cases are due to exogenous contamination. Peckham reports a series of 545 cases of puerperal infection in which intra-uterine cultures were obtained in about 60 per cent; in this group *Cl. welchii* were found in only 0.62 per cent of those cultured. The organisms do not thrive in the blood stream, being obligate anaerobes; positive blood cultures and metastatic foci are usually detected but a short time before the death of the patient.

2. There is evidence to warrant the belief that a cervical erosion is in the nature of a physiologic manifestation of the endocervium due probably to hormonal stimulation and not necessarily a pathologic entity.

3. A cause and effect relationship or even a predisposing kinship between commonly recognized cervical disorders and cancer is by no means consistent nor proved (leucoplakia excepted).

4. Justification for the radical therapy characterizing the present scramble for cervical prophylaxis needs to be more clearly established.

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THE SIGNIFICANCE OF CLOSTRIDIUM WELCHII IN THE GENITAL TRACT OF PREGNANT AND PUERPERAL WOMEN*

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GAS bacillus infections in relation to pregnancy have long been recognized; the clinical picture, treatment, and gravity of such infections are now fairly well understood. The object of this paper is to ascertain the significance of *Clostridium welchii* when found in the genital tract of pregnant and puerperal women, regardless of whether or not the patients presented a true gas bacillus infection.

Ledue, in 1579, reported a case of puerperal infection in which, from his description, the causative organism could have been none other than the gas bacillus. It was not until 1892 that Welch and Nuttall isolated the *Bacillus aerogenes capsulatus*. Later many other names were applied to the same organism. Welch bacilli are found frequently in anaerobic cultures from human and animal feces. When these bacteria can be cultured from the intestinal tract it is little wonder that they may be found in the vagina. The gas bacillus is commonly and readily

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The 5 patients who had positive cultures in the prenatal clinic showed no evidence of infection or morbidity in the puerperium.

Of the 19 patients who had a positive culture in the puerperium, only 8 showed morbidity, i.e., a fever of 100.4° F. or over at some time. Five of these had evidence of endometritis and the Welch bacillus was cultured from the genital tract. Of these 5 only 1, the patient who died, presented the typical picture of gas bacillus sepsis. The remaining 4 showed symptoms and signs of ordinary puerperal endometritis.

During the fifteen years previous to this study there had been only one other case of infection due to *Cl. welchii* recorded at Sloane Hospital for Women. This was a patient with an early incomplete abortion who developed a typical Welch bacillus bacteremia. She exhibited high fever, cyanosis, jaundice and extreme prostration for several days. Gas bacilli were recovered from the vagina and blood stream. This patient received antitoxin and recovered completely in three weeks.

DISCUSSION

The incidence of positive *Cl. welchii* cultures in routine cases was 4.5 per cent which is higher than other investigators have reported. Five of the total 25 positive cases developed a true infection by the organism. In 4 cases the infection was localized in the genital tract, and in one only did the infection become generalized. While the virulence of the organism was not studied, nevertheless a clue as to relative and potential virulence may thus be obtained. The 4 patients with endometritis all received antitoxin and local treatment with zinc peroxide; these made uneventful recoveries. The virulence here may have been mild or the treatment completely successful.

The finding of *Cl. welchii* in the vagina in 4.5 per cent of the total series may indicate nothing more than contamination of the vagina from the perineum and anus. Approximately 80 per cent of the positive cultures were found in patients in labor or in the early puerperium, yet the potential danger is quite obvious when 20 per cent of these patients developed puerperal endometritis, and the only organism recovered was the Welch bacillus.

In the 5 infected patients 3 had living infants. Other workers have claimed that the death of the fetus hours before delivery is partially responsible for *Cl. welchii* becoming pathogenic. A focus of traumatized tissue was present, however, in all 5; there being 2 abortions, 1 cesarean section, and 2 deliveries with forceps and episiotomy. The 4 cases of puerperal endometritis had none of the clinical stigmas of *Cl. welchii* sepsis, so that the etiology depended on anaerobic culture for verification.

SUMMARY

1. In 547 routine cases of pregnant and puerperal women positive *Cl. welchii* vaginal cultures were obtained in 4.5 per cent.

2. Of the patients with positive cultures, 20 per cent showed puerperal morbidity and clinical evidence of at least an endometritis.

In 1935 at Sloane Hospital for Women, two cases of *Clostridium welchii* infection were seen on the wards at practically the same time.

1. The first patient was a multiparous woman of 39 years who was admitted to the hospital with a history strongly suggestive of a criminal abortion at two months. For two weeks she ran an afebrile course, with scanty vaginal bleeding. She then developed a low grade temperature, and anaerobic cultures from the vagina revealed *Cl. welchii*. At the end of another two weeks a definite abscess had developed in the right broad ligament, pointing abdominally in the groin. The abscess was opened surgically and anaerobic cultures showed a pure strain of *Cl. welchii*. This patient made an uneventful recovery following antitoxin treatment and the local use of zinc peroxide by Dr. Frank L. Meleney on the surgical service.

2. During the early hospitalization of the above patient a 25-year-old primigravid woman was admitted to the ward at term for observation and treatment of a pre-eclamptic toxemia. After two weeks, termination of the pregnancy was thought advisable, and she was successfully induced with castor oil and quinine. Following ten hours of labor, with membranes ruptured for five hours, a medium forceps delivery with episiotomy was done. The baby was in good condition. A few hours after delivery the patient seemed to be in shock; a transfusion was given without relief. The patient remained in a semicomatose condition with a high fever, suggesting an overwhelming sepsis, and she died forty-eight hours after delivery. Anaerobic vaginal cultures taken in the brief post-partum period and an anaerobic blood culture obtained sixteen hours before death were later positive for *Cl. welchii*. Post-mortem examination confirmed the diagnosis of gas bacillus bacteremia, there being numerous metastatic foci of infection.

The drainage of the abscess in the first patient and the death of the second patient came four days apart. These patients were in separate isolation units of the hospital and cross-infection seemed unlikely. Nevertheless a thorough but unsuccessful study was carried out in an attempt to find a possible cross-infection.

This experience led to the taking of anaerobic vaginal cultures on all patients in the hospital at the time. Then for several days each admission to the wards or labor room was anaerobically cultured. Later, cases were studied early in labor, on the third post-partum day, and in the prenatal clinic. In all, 547 patients were examined and positive *Cl. welchii* cultures were obtained in 25, or approximately 4.5 per cent. Well over half of the cultures were taken from the cervix through a sterile speculum, the remainder from the lower vagina by carefully separating the labia. All cultures were made on dry swabs and inoculated on blood agar plates for aerobic and anaerobic incubation. The swabs were then placed in dextrose meat media for anaerobic culture. Incubation was carried out from one to several days in the search for anaerobic growth. Identification of the organism was made by direct smear and the "double zoning effect" of colonies on the anaerobic blood agar plates.

The culture material for the series was obtained under the following conditions:

77 cases ante partum or post partum in the wards at the same time as the fatal case	9 positive cultures (all post partum)
42 patients on admission to the labor room	1 positive culture
133 patients on the third day of the puerperium	10 positive cultures
73 patients cultured both ante partum and post partum	0 positive cultures
222 patients cultured in the prenatal clinic	5 positive cultures
547 total cases	25 positive cultures